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CELLULAR INCLUSIONS IN CEREBRAL LESIONS OF EPIDEMIC ENCEPHALITIS

SECOND REPORT *

JAMES R. DAWSON, JR., M.D.

NASHVILLE, TENN.

Encephalitis is a term which has been applied to a wide variety of diseases of the central nervous system. The clinician uses this term to designate an obscure, diffuse disease of the brain, whether of proved inflammatory nature or not. The pathologist employs it to denote any condition in which there is objective evidence of cerebral inflammation. Three large subdivisions have been made on an etiologic, pathologic and clinical basis. These are the toxic or hemorrhagic, the bacterial or suppurative and the nonhemorrhagic nonsuppurative types. The toxic form may be recognized with some certainty clinically and pathologically, because it is often possible to link intoxication with arsenic, guanidine, lead and other poisons with the onset of clinical symptoms referable to the central nervous system and because hemorrhages and other changes in the brains are found at autopsy. The bacterial form may be established by cultivation of micro-organisms from the injured cerebral tissues and by the histologic characteristics of the lesions.

The nonsuppurative, nonhemorrhagic group includes a wide variety of specific and nonspecific types, among which are the postinfectional and postvaccinal forms and epidemic encephalitis. This grouping is clinical rather than anatomic, because in most instances the histologic features of the associated lesions provide an inadequate basis for a subdivision purely on the grounds of the pathologic observations. Of the various types, epidemic encephalitis is probably the most important, because of its relatively high incidence and disabling sequelae.

In von Economo's original description and in numerous articles since, epidemic encephalitis is depicted as a disease of days' or years' duration, which may end in complete or partial recovery, terminate fatally in the early stages or be intermittently progressive and finally

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From the Department of Pathology, Vanderbilt University School of Medicine.

end in death.[1] Subjective symptoms and objective signs run the gamut of neurologic and psychiatric changes. Examination of the blood and spinal fluid is not more conclusive; finally, at autopsy, the brains may show acute necrosis of ganglion cells, small hemorrhages, edema, neuronophagia, glial scars, general loss of neurons, perivascular cuffs of round cells and other nonspecific changes. The distribution of these lesions is not characteristic. Although the basal ganglia are said to be most commonly involved, the cortical cells are frequently severely damaged. It is obvious that cases of epidemic encephalitis vary widely; nevertheless, the group is still considered a clinical, pathologic and etiologic entity.

Attempts to demonstrate a causative agent in epidemic encephalitis have been unsuccessful. Pleomorphic streptococci have been cultivated by von Wiesner [2] and Rosenow,[3] but definite proof is still lacking in regard to the relation of these organisms to the disease. Other bacteria have been cultivated, but their etiologic significance is even less convincing. A filtrable virus was mentioned as a possible etiologic factor soon after the discovery of the disease, and when Doerr and Vöchting [4] observed that disturbances of the central nervous system which were associated with ganglionic necrosis frequently developed in rabbits suffering from herpetic keratitis, many investigators drew a hasty analogy between herpetic and epidemic encephalitis. Several strains of herpes simplex virus and one of rabies virus have been isolated from the brains and nasopharyngeal washings of patients who died of clinical epidemic encephalitis. The workers who isolated these viruses explained the frequent or nearly universal failure of most investigators to transmit the infection to experimental animals on the basis of autosterilization of the virus or the absence of some necessary predisposing factor. Considerable doubt was cast on the etiologic significance of herpes simplex virus in epidemic encephalitis for several reasons, especially when Flexner and Amoss [5] reported the isolation of this virus from the spinal fluid of a patient with syphilis in whom

1. von Economo, C.: Encephalitis Lethargica: Its Sequelae and Treatment, New York, Oxford University Press, 1931. Tilney, F., and Howe, H. S.: Epidemic Encephalitis (Encephalitis Lethargica), New York, Paul B. Hoeber, Inc., 1920. Epidemic Encephalitis: Report of a Survey by the Matheson Commission, New York, Columbia University Press, 1929; Second Report of a Survey by the Matheson Commission, ibid., 1932.

2. von Wiesner, R.: Die Aetiologie der Encephalitis lethargica, Wien. klin. Wchnschr. **30**:933, 1917.

3. Rosenow, E. C.: Streptococci in Relation to the Etiology of Encephalitis Lethargica, J. Infect. Dis. **34**:329, 1924.

4. Doerr, R., and Vöchting, K.: Etudes sur le virus de l'herpès fébrile, Rev. gén. d'opht. **34**:409, 1920.

5. Flexner, S., and Amoss, H. L.: Contributions to the Pathology of Experimental Virus Encephalitis; an Exotic Strain of Encephalitogenic Virus, J. Exper. Med. **41**:215, 1925.

they found no evidence of herpes or encephalitis. From this observation it seemed that the virus recovered from the brains of patients suffering from encephalitis may have been adventitious. In spite of the inability of most workers to recover any virus from patients with epidemic encephalitis, this malady has been placed in the group of virus diseases by several investigators.[6]

Many of the virus diseases are associated with specific cellular changes in the form of inclusion bodies, which are regarded as the characteristic feature of the lesions. This is especially true of herpetic lesions, including the encephalitis of rabbits. In support of the assumption of a virus as the etiologic agent, various workers have described inclusion bodies within the nuclei or cytoplasm of cells of the central nervous system in cases of epidemic encephalitis. The most important of these will be described briefly.

Levaditi's [7] inclusions, as illustrated in an article by him, are present within degenerating pigmented ganglion cells. They are large and indistinct. The nucleus is not seen, so it is impossible to determine the relationship of the inclusions to it. In the brains of rabbits that had died of encephalitis produced by the injection of emulsified brain or saliva of patients who had died of this disease, he was able to demonstrate small round or oval eosinophilic intranuclear inclusion bodies, which at times appeared to possess a *structure interne*. These he interpreted as typical herpetic inclusions.

Omorokow [8] described inclusion bodies in ependymal cells in the brains of patients who had died of epidemic encephalitis:

> They are two or three times smaller than the nucleolus, sometimes regularly round, sometimes angular. In Nissl preparations they take a light green or dark blue color. In the latter case one is able to see in the central portions unstained granules which form separate inclusions. In Lentz preparation of paraffin sections these inclusions are brought out especially sharply. At first glance they resemble quite closely corpora amylacea. By this method the inclusions stain a pale rose color and are multiform, being small round granules, half moons, ring-shaped or appearing as two half moons juxtaposed. Many times the inclusions have a granular inner portion.

Omorokow and Luksch [9] each described inclusions in nerve cells; the inclusions are similar, so the two descriptions will be combined and Omorokow will be quoted:

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6. Rivers, T. M.: Relation of Filtrable Viruses to Diseases of the Nervous System, Arch. Neurol & Psychiat. **28**:757 (Oct.) 1932.

7. Levaditi, C.: Ectodermoses neurotropes, poliomyélite, encéphalite, herpès, Paris, Masson et Cie, 1922.

8. Omorokow, L.: Zur Frage der pathologisch-anatomischen Veränderungen bei den chronischen Formen der epidemischen Encephalitis, Ztschr. f. d. ges. Neurol. u. Psychiat. **104**:421, 1926.

9. Luksch, L.: Ueber "Ganglienzelleinschlüsse" bei Encephalitis epidemica von Economo, Beitr. z. path. Anat. u. z. allg. Path. **71**:201, 1922.

The inclusions which we observed in nuclear alterations conform in an obvious manner to those which were described by Luksch. He found in the nuclei of pigmented nerve cells of patients dead of encephalitis lethargica peculiar inclusions which were more often round than oval, occasionally multiple but usually single. These inclusions were smaller than the nucleolus, homogeneous, without inner structure, sharply outlined, and by the Lentz method they take a brownish-golden stain. They are not stained by the methyl green-pyronin method of Unna-Pappenheim. They remain as colorless bodies close to the red nucleolus. These inclusions closely resemble those described in Borna disease of horses. They are similar in size, shape and staining reaction by Lentz' method.

The inclusions last described were also found in ganglion cells of patients who died of hepatic cirrhosis, endocarditis, peritonitis and tuberculosis. Luksch considered them to be products of cellular degeneration rather than specific reactions to a virus. He found them in the pigmented ganglion cells of the substantia nigra. Omorokow described them in the nerve cells of the subcortical ganglia. It is mentioned that these investigators observed the nuclear and nucleolar degenerative changes in one case of epilepsy in which there was circumscribed encephalitis. In numerous other cases of encephalitis they were unable to demonstrate similar inclusions.

Herzog[10] found round, oval or pear-shaped inclusions within the nuclei and cytoplasm of ganglion cells in the region of the fourth ventricle. These were also observed free in the tissues. They stained red by Giemsa's method. No photograph or drawings accompanied his article.

Volpino and Desderi,[11] Dafano,[12] Ottolenghi, Tonietti and d'Antona[13] and Meleney[14] described granules within the cytoplasm of ganglion cells. These are not analogous to the inclusion bodies found in any known virus disease, and it is probable that they are products of degeneration, perhaps in the form of lipochrome or prelipochrome pigment. The intranuclear bodies described and illustrated in articles by Omorokow and Luksch resemble to a certain extent those seen in virus diseases, especially in Borna encephalitis of horses. However, these investigators showed that similar bodies could be demonstrated in pigmented ganglion cells of the pons in conditions other than encephalitis. Consequently it is difficult to attach much significance to them.

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10. Herzog, G.: Zur Pathologie der Encephalitis epidemica, Verhandl. d. deutsch. path. Gesellsch. **18**:294, 1921.

11. Volpino, G., and Desderi, P.: Osservazioni microscopiche supra i cervilli in alcuni casi di encefalite epidemica, Ann. d'ig. **30**:81, 1920.

12. Dafano, C.: The Histopathology of Epidemic (Lethargic) Encephalitis, Brit. M. J. **1**:153, 1921.

13. Ottolenghi, D.; Tonietti, F., and d'Antona, S.: Ricerche sulla eziologia e patogenesi dell'encefalite letargica, Atti d. r. Accad. d. fisiocrit. in Siena **12**:79, 1920.

14. Meleney, H. E.: Degeneration Granules in Brain Cells in Epidemic Encephalitis, Arch. Neurol. & Psychiat. **5**:146 (Feb.) 1921.

Levaditi's inclusions, as pictured, are difficult to interpret. The colored illustrations are of degenerating ganglion cells, and the nucleus is not seen. It is impossible to make out any structure which might be considered an inclusion simulating those of herpes simplex. He described and illustrated *neurocorps encéphalitiques*, which are not typical of herpetic inclusions, in the neurons of rabbits suffering from encephalitis induced by the injection of material from patients with this disease.

Notwithstanding the large number of cases of epidemic encephalitis that have been studied, no distinctive cellular changes characteristic of virus diseases have been reoprted from other laboratories. This may be due to failure to examine all parts of brains carefully, to faulty technic or to failure to recognize the changes, or the inclusion bodies may not have been present at the time of autopsy.

REPORT OF CASES

In a case recently reported from this laboratory,[15] in which the condition was diagnosed as epidemic encephalitis clinically, intranuclear and intracytoplasmic inclusion bodies were described in the neurons and neuroglia cells. The intranuclear inclusions were thought to be characteristic of those seen in virus diseases. The intracytoplasmic bodies were thought to be degenerative in nature.

A brief summary of the protocol of this case follows:

A white boy, aged 16 years, entered the hospital on July 18, 1931. His mother thought that he had suffered a sunstroke. Sixteen months previously he had been found on the street in an unconscious condition. Twelve months previously, while at a camp, he was said to have suffered a sunstroke. At that time he was found to have a temperature of 99 F. and clear spinal fluid with 14 cells. Since then he had exhibited a tendency to a reversal of the sleep cycle and had shown some psychic changes. A week before admission he began to have involuntary jerking movements of the arms and legs. While in the hospital he had to be placed in isolation because he persisted in playfully throwing an infant roommate into the air and catching him. At one time he took a large block of ice which was being used to cool the room in bed with him and proceeded to gnaw at it.

Examination.—The following points were noted: temperature, 99 F.; pulse rate, 32; respiratory rate, 20. Voluntary movements were slow, and the expression was masked. There were frequent involuntary jerking movements of the arms and legs, and typical lead-pipe rigidity of the extremities was observed. One observer noted the presence of labial herpes on July 29, but made no further notes regarding it. The spinal fluid was clear, was under slightly increased pressure and contained 14 cells; the spinal fluid sugar was 58 mg.; the Wassermann reaction of the fluid was negative.

Histologic Study.—Grossly, the brain showed congestion and edema. Microscopically, there was congestion of the vessels throughout, with some capillary

15. Dawson, J. R., Jr.: Cellular Inclusions in Cerebral Lesions of Lethargic Encephalitis, Am. J. Path. **9**:7, 1933.

hemorrhage and infiltration by epivascular lymphocytes. These changes were most striking in the cortex, the lenticular, caudate and red nuclei and the thalamus. In addition, there were diffusely distributed, isolated, necrotic nerve cells. Accompanying these degenerative changes there were many compact, more or less granular, eosinophilic inclusion bodies within the nuclei. Refractile, hyaline, eosinophilic bodies were seen in the cytoplasm. Similar intranuclear inclusions were observed in swollen glia cells. In addition to these acute changes, glial rosettes, some of which surrounded fragments of calcium, were seen. The distribution of these lesions was comparable to that of the vascular lesions.

It was thought at the time this case was reported that the presence of intranuclear inclusions, which are characteristic of certain virus diseases, within the nerve and neuroglia cells in the brain of a patient who had died of clinical epidemic encephalitis was of considerable importance, especially as no similar inclusions had been found in other similar cases in this or other laboratories. Because of the presence of the distinctive cytopathologic lesion it was judged that this case should be considered as an instance of a specific type of encephalitis and that it should be distinguished in the group of epidemic encephalitis. Since this report a similar case was studied in this laboratory:

M. R. K., a white girl, aged 5 years, was first seen in the hospital on Oct. 4, 1928, at the age of 9 months because of contact with tuberculosis. She was well at that time and remained healthy until October, 1932. She was then brought to the hospital by her mother, who said that for one month the child had had a "breaking out" over the body, which had recently become worse. Four days previously she suddenly awoke at night laughing and crying alternately; she had numerous hallucinations of birds and animals. The mother did not think that the child had fever at that time. Since then (the time of onset is unknown) the patient had exhibited peculiar jerking movements of the extremities.

Physical examination revealed only eczema and scabies, for which she was treated. During the examination she was seen to jerk her arms once or twice. She was not seen again until Jan. 2, 1933. The mother stated at this time that the jerking movements had become more frequent and more severe. During the six weeks before this admission bedwetting had become habitual. She had gradually lost the ability to speak and had become so stuporous that she did not eat. The involuntary jerking movements had become so severe that she frequently injured her face when the arms were suddenly flexed. At times the movements had been so rapid that she appeared to tremble. Inability to speak was preceded by a period during which she seemed to mumble. For six weeks she had been confined to bed because of inability to control her muscles. She had never vomited or complained of headache.

Physical Examination.—The temperature was 97.8 F.; the pulse rate, 72, and the respiratory rate, 20. The patient was a filthy, undernourished white girl who lay in bed in no characteristic position. She was lethargic. There was a maculopapular eruption over the body, which was most marked on the face. The neck was neither retracted nor stiff. The eyes were not remarkable. There was no strabismus or irregularity of the pupils. The reaction to light was sluggish. The chest was symmetrical. The lungs were clear. Respiration was of the Cheyne-Stokes type. The abdomen was not remarkable. The extremities were emaciated.

The muscles were hypotonic, and no reflexes were obtained. Kernig's sign was not present. There was no clonus. The involuntary movements consisted of sudden flexion of the arms or legs, sometimes of both.

Laboratory Findings.—Blood: Red cells numbered 5,950,000 and white cells, 9,200. There were 12 Gm. of hemoglobin per hundred cubic centimeters, 47 per cent polymorphonuclears and 18.5 per cent eosinophils. The Wassermann reaction was negative. The urine was normal. The spinal fluid was clear, with a slightly increased or normal pressure; there was a trace of globulin and from 2 to 4 cells per cubic millimeter. The Wassermann reaction was negative, and the reaction to 0.1 mg. of old tuberculin was negative. On January 3 the blood and spinal fluid sugar were 88 and 61 mg., respectively.

Course in Hospital.—Treatment consisted of forced feedings and the application of sulphur ointment to the cutaneous lesions. The stupor increased progressively, as did the involuntary muscular movements. The temperature, which was subnormal at the time of admission, rose higher each day until it reached a maximum of 107.4 F. at the time of death. No changes in the reflexes were noted. A questionable Babinski sign was present bilaterally. The extremities gradually became stiff, exhibiting characteristic lead-pipe rigidity before death, which occurred on January 24.

Pathologic Anatomy.—Gross and microscopic examination of organs other than the central nervous system revealed nothing except bronchopneumonia.

Grossly, the meninges appeared smooth, thin and glistening. There was considerable congestion of the vessels, and occasionally one saw small questionable areas of hemorrhage into the subarachnoid space. There was a very slight increase in the amount of subarachnoid fluid. This fluid was clear and colorless. Sections of the brain revealed diffuse congestion and edema, with a few questionable areas of hemorrhage. These changes were diffuse and involved the gray and white matter. They were perhaps slightly more prominent in the gray matter of the cortex and basal ganglia.

Microscopically, the vessels of the subarachnoid spaces appeared congested. One was able not infrequently to find small hemorrhages within the sheaths of these vessels and also within the subarachnoid space. Small numbers of lymphocytes, mononuclear leukocytes and plasma cells were also present. There was a slight thickening of the pia-arachnoid over the pons.

Within the brain there were vascular lesions of a nonspecific nature. The perivascular spaces were unusually prominent, and the vessels were congested. There were a few small areas of hemorrhage. In some instances the endothelial cells were swollen. Around and within the walls of the smaller arteries and veins one saw quite a few lymphocytes, monocytes and an occasional plasma cell. In addition to these, there were a few cells which remain unclassified: they were round, oval or spindle-shaped; their nuclei were relatively large, and within them one saw numerous coarse chromatic granules. The nucleoli were not prominent. Although these lesions occurred in the white matter, they were seen much more frequently in the gray matter.

The nerve cells were considerably altered in appearance. They were affected individually, so that it was not uncommon to find two cells side by side, one apparently normal, the other exhibiting degenerative changes which varied from the milder types to actual necrosis. These changes were of various types; simple swelling of the nucleus and cytoplasm of the cell was apparently the simplest form. Again, the cells were so shrunken that it was difficult to distinguish the nucleus and nucleolus. In hematoxylin and eosin preparations the cells stained a homogeneous reddish purple. The perineural space of such a cell was large.

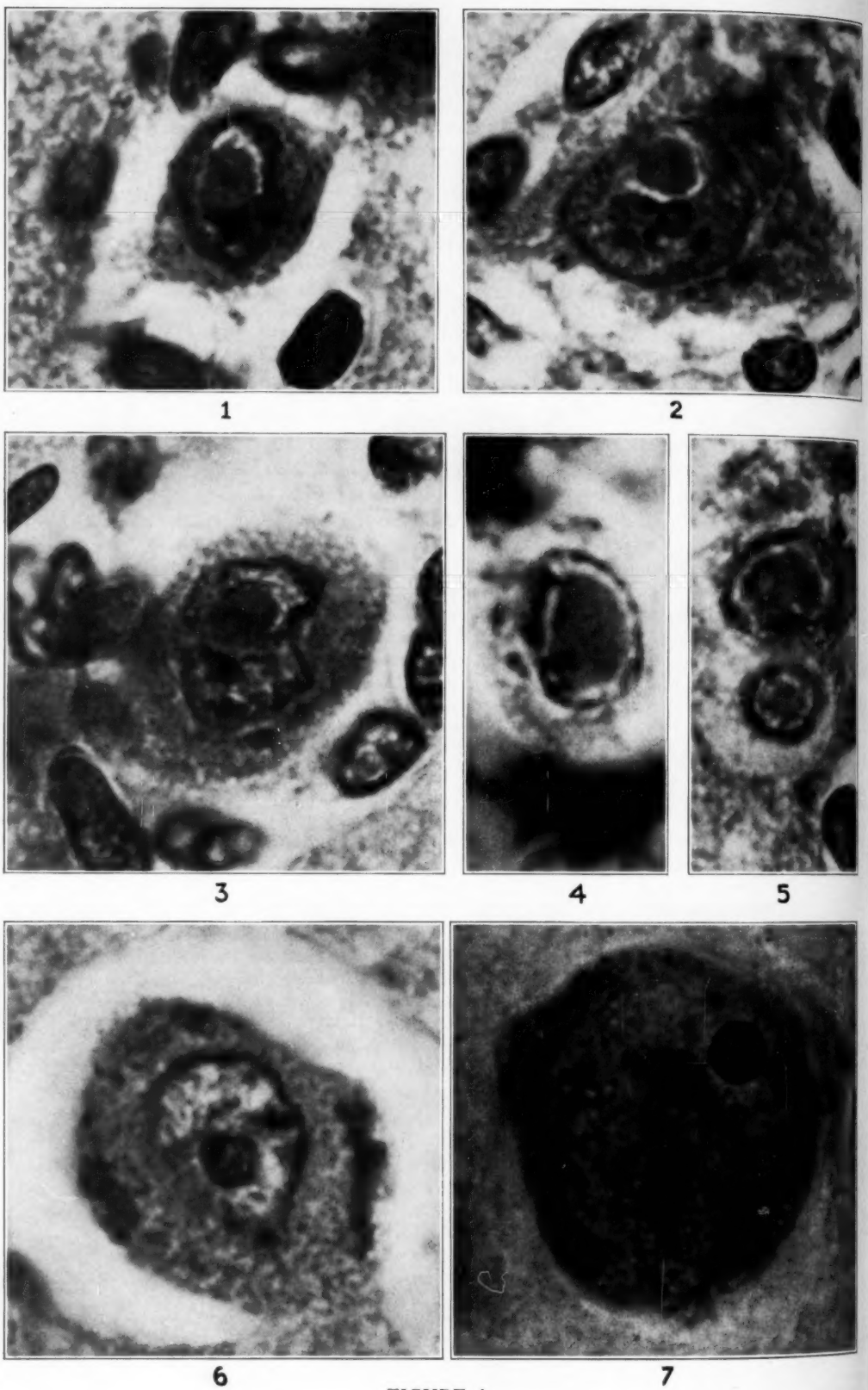
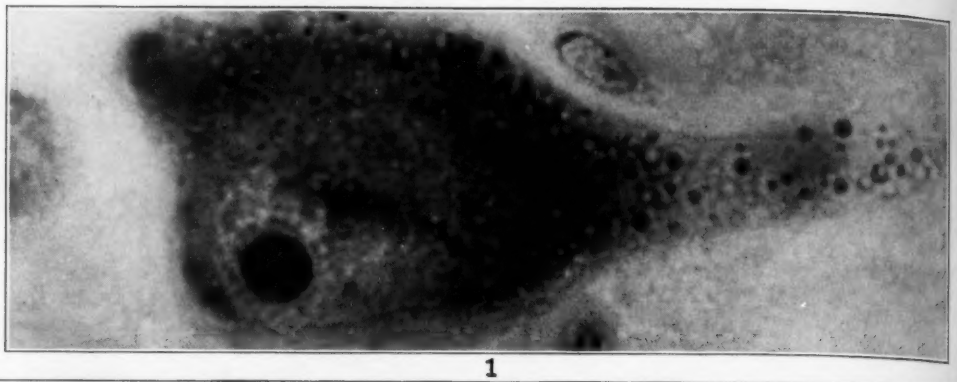


FIGURE 1

EXPLANATION OF FIGURE 1

Fig. 1.—*1*, neuron of the cortex showing a large granular intranuclear inclusion which is surrounded by a zone devoid of chromatic material. Phagocytic cells are seen around the neuron. Hematoxylin and eosin stain; × 2,300. *2*, ganglion cell of the caudate nucleus showing a relatively small, round granular intranuclear inclusion which is surrounded by a halo. The nucleolus is easily distinguishable from this inclusion. Pseudoneuronophagia is evident. Hematoxylin and eosin stain; × 2,300. *3*, swollen cortical neuron showing a round, granular intranuclear inclusion, condensation of chromatic material along the nuclear membrane and neuronophagia. Hematoxylin and eosin stain; × 2,300. *4*, neuron of the insular cortex showing a large, well defined, granular intranuclear inclusion with the characteristic clear halo and conspicuous nuclear membrane due to condensation of chromatic material along it. Hematoxylin and eosin stain; × 2,300. *5*, neuron (above) showing a typical intranuclear inclusion and neuroglia cell (below) with an intranuclear inclusion which is out of focus. *6*, neuron of lenticular nucleus showing loss and peripheral dispersion of Nissl substance, swelling of the nucleus and loss of chromatic material. *7*, ganglion cell of the pons showing the refractile cytoplasmic droplets illustrated in *1* and *2* of figure 2. These are so numerous that they obscure the nucleus.



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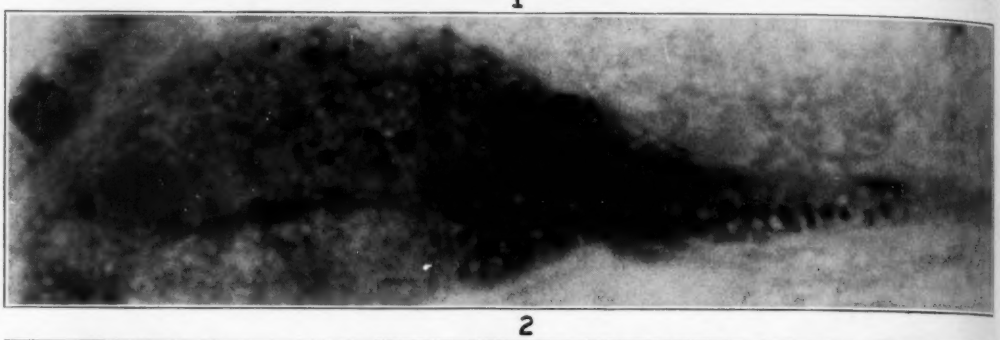

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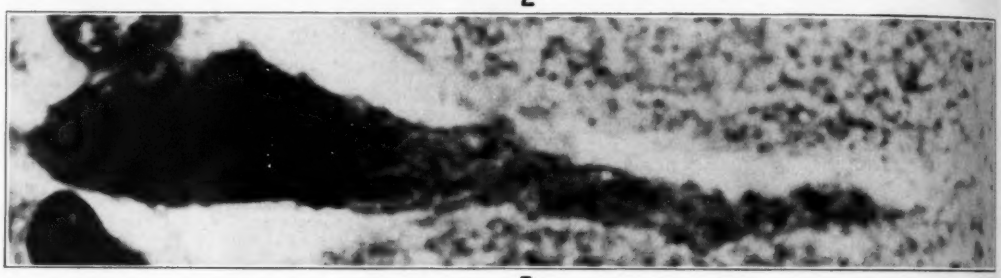

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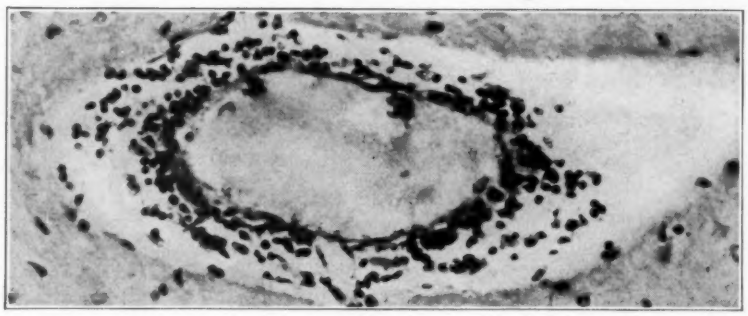

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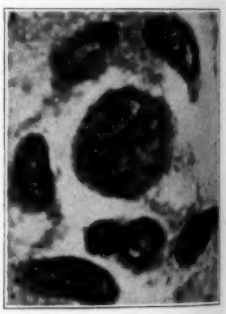

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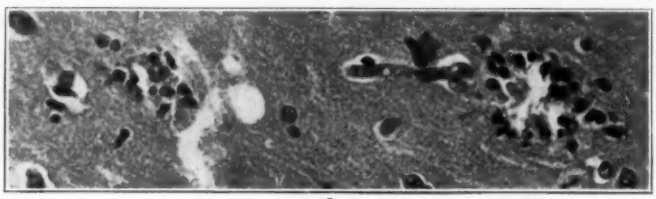

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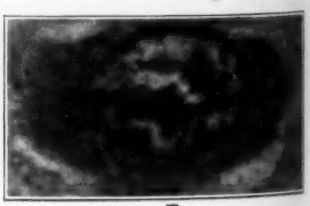

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FIGURE 2

EXPLANATION OF FIGURE 2

Fig. 2.—*1*, large pigmented ganglion cell of the pons showing small refractile droplets within the cytoplasm of the cell body and its processes. The granular, vacuolated nucleoli are also illustrated. Hematoxylin and eosin stain; × 2,300. *2*, ganglion cells showing changes similar to those in the cell in *1*. *3*, neuron of the insular cortex showing shrinking of the nucleus and cytoplasm. Hematoxylin and eosin stain; × 2,300. *4*, small venule of the thalamus showing infiltration of its sheath and perivascular space by round cells. *5*, neuron of the caudate nucleus showing an ovoid intranuclear inclusion. There is also some neuronophagia. Hematoxylin and eosin stain; × 750. *6*, two glial rosettes of the pons. Hematoxylin and eosin stain; × 500. *7*, neuron of the cortex showing swelling of the nucleus and dissolution of the chromatic material, with focal accumulations of chromatic granules along the nuclear membrane.

In many of the swollen cells the nucleus was eccentric and there was loss of Nissl substance; that which remained was distributed peripherally. Associated with the loss of Nissl substance there was usually some dispersion of the nuclear chromatic material, with focal accumulations of this substance along the nuclear membrane. The nucleoli were large and vacuolated.

There was an increased amount of pigment in many cells. This change was especially evident in the pigmented ganglion cells of the pons. In eosin-methylthionine chloride (methylene blue) preparations one saw large clumps of small greenish, yellowish or reddish granules, which displaced and obscured the nucleus in many instances. Quite commonly these accumulations of pigment granules were arranged in a compact mass. In such cases they were usually uniform in size. In many cells the pigment was distributed throughout the cell, extending out into the processes. It was not uncommon to see brilliant red, well outlined, refractile droplets within the cytoplasm of the cells. Many were slightly larger than pigment granules; others were one-third or one-half the size of the nucleolus. They extended far into the cellular processes, so that at times they appeared to lie extracellularly. In many instances they appeared to be surrounded by a halo. In sections stained by Goodpasture's carbol-aniline-fuchsin-methylthionine chloride method they appeared more brilliantly red, but otherwise they were identical. They did not possess an inner structure in the form of vacuoles or basophilic granules. In many instances the glia cells appeared swollen, but there was no necrosis. The ependymal epithelial cells were not remarkable.

Associated with these nonspecific cellular changes one found inclusion bodies which were thought to be characteristic of a virus lesion. These inclusions were present within the nuclei of nerve and glia cells. In eosin-methylthionine chloride preparations they appeared as round, oval or irregularly outlined, well defined, pinkish masses. They were single or multiple. Many were scarcely larger than the nucleolus, while others almost filled the swollen nucleus. They were either homogeneous or granular. The larger ones were usually more homogeneous and stained less distinctly. They were easily distinguished and entirely separate from the basophilic, vacuolated nucleoli. These intranuclear bodies were almost invariably surrounded by a zone which was devoid of chromatic material. Affected cells always showed some decrease in the amount of nuclear chromatic material. The nuclear membrane was unusually distinct because of condensations of this material along it.

These inclusions were never found in cells which did not show some degenerative changes, and it was not at all uncommon to find them in necrotic cells the nuclei of which were no longer demonstrable. Such cells were surrounded or actually invaded by round, oval or spindle-shaped cells with pale bluish-pink cytoplasm and relatively large nuclei. Although it was not common, one was able occasionally to find such a phagocytic cell which contained within its nucleus a relatively small, granular, eosinophilic inclusion body. Inclusions similar to those already described were found within the nuclei of glia cells. However, they were not as common as those within the nuclei of nerve cells.

In sections stained with eosin and hematoxylin or with methylthionine chloride, many of the nerve cells which were degenerated contained within their cytoplasm round or oval, refractile, hyaline pinkish masses. Some of these were no larger than the nucleolus; others were two or three times the size of this structure. Frequently they were surrounded by halos. All these smaller cytoplasmic masses were sharply outlined. One saw other masses similar in color and density which filled a large portion of the cytoplasm. These were irregular in outline and poorly defined. It was thought that these masses were products of cellular

degeneration. In unstained preparations they were colorless. They did not stain by Goodpasture's carbol-aniline-fuchsin-methylthionine chloride method. These properties indicated that they were probably neither derivations nor precursors of pigment.

The specific and nonspecific cellular lesions, with their associated cellular reaction, and the vascular lesions were distributed throughout the brain. Sections from various cortical areas presented widely different pictures. All the lesions were seen, but the acute and subacute lesions were most prominent. The basal ganglia showed similar variations in degree of involvement. In general, the older type of lesion predominated, and inclusion bodies were less numerous. In the pons and medulla there was a striking admixture of acute and chronic inflammatory changes, which were associated with extreme cellular necrosis and numerous inclusions. The cornu ammonis showed only congestion and edema. No specific changes were seen in the cerebellum. In the cord one saw a few lymphocytes, plasma cells and mononuclear leukocytes within the vessel sheaths, perivascular spaces and subarachnoid space. No cellular necrosis or inclusions were seen. There were some congestion and edema but no hemorrhage.

COMMENT

The distinctive feature of these cases of epidemic encephalitis is the presence in the brain of intranuclear inclusion bodies of the type seen in other virus diseases. It is thought that this distinct cytopathologic lesion is evidence of virus activity. The inclusions resemble to a certain extent those of herpes simplex and others. Although they are similar to the inclusions in herpes simplex, one can conclude that they are not herpetic, since rabbits, which are highly susceptible to the virus of herpes simplex, showed no lesions following intracerebral, subcutaneous and corneal inoculations of brain tissue from each patient. The pathologic lesions differ from those of experimental herpetic encephalitis in that they are more diffuse and are not accompanied by such extensive necrosis. One is justified in assuming that these specific cellular changes are evidences of virus activity and that these cases of encephalitis were due to an unknown virus.

It is not unexpected that all attempts to transmit this disease to rabbits, mice, rats, monkeys, dogs, cats and chickens by intracerebral, intraperitoneal, subcutaneous and corneal inoculations of brain tissue were unsuccessful, since many well recognized or suspected virus diseases have not been engrafted on foreign hosts. On examination of the brains of supposedly rabid dogs in this laboratory, many cases of nonrabic encephalitis have been found. In several of the brains well defined inclusions were found within the nuclei and cytoplasm of nerve and glia cells. All attempts to transmit this disease to rabbits and dogs have been unsuccessful.

In spite of evident differences, one is impressed by certain points of similarity between the clinical courses in the cases reported in this article. In each the onset was rather sudden, without any definite prodromal symptoms and without much elevation of temperature. In the first case

the patient lost consciousness suddenly, while in the second the patient awoke from sleep in a state of acute hallucinosis and excitement. In the first case there were two sudden recurrences of the attacks, while in the second there was none. Following the initial attack psychic and motor evidences of progressive cerebral injury appeared in both cases. In the first patient there were reversal of the sleep cycle, slowing of voluntary motor activity and, finally, sudden, involuntary, convulsive jerkings of the arms and legs. In the second patient there were attacks of hysterical laughing and crying, involuntary, convulsive jerking movements and loss of speech. In both cases the condition developed finally into so-called postencephalitic parkinsonism, with a masklike expression and lead-pipe rigidity. The spinal fluid was similar in the two cases; in the first, the cell count varied from 14 to 6; in the second, from 2 to 4. The sugar was 58 mg. in the first patient and 61 in the second. The manner of death is the most striking feature. In each case the temperature began to rise gradually over a period of from seven to ten days, finally reaching a maximum of 107.4 or 106 F. at the time of death. The patients were lethargic while in the hospital, and the condition became progressively worse. In each patient cutaneous lesions were noted—in the first, labial herpes; in the second, scabies and eczema. The significance of these is not apparent.

Notwithstanding the varied symptomatology and the physical and laboratory observations, including the examination of tissues removed at autopsy in cases of epidemic encephalitis, there are certain findings common to both of these cases which are not characteristic of any of the various types of epidemic encephalitis which have been described.

Clinically, the sudden onset, with loss of consciousness and hallucinations, followed by the rapid development of hyperkinesia and parkinsonism, and high fever followed rapidly by death, when taken together, are certainly uncommon. This is also true of the lethargy, which did not develop until relatively late in the disease, and of the absence of weakness of the extra-ocular muscles. Although there was diplopia in the first case, ocular palsy was never noted.

The observations at autopsy are of the greatest importance. In these two patients there were glial scars indicative of an older process; the epivascular lymphocytic infiltration pointed to a more recent inflammatory process, and, lastly, the acute necrosis of ganglion cells was evidence of recent injury. In each case the changes were focal and were distributed throughout the brain. The more acute ones were most numerous in the cortex; the subacute and chronic ones were most numerous in the basal ganglia, the medulla and the pons. Capillary hemorrhage and edema were also evidences of the more acute process. This picture is entirely compatible with a diagnosis of chronic encephalitis which is intermittently progressive, and there is no doubt that a diagnosis of

chronic and acute epidemic encephalitis should have been made. The widespread distribution of the lesions explains well the signs of cortical and subcortical injury which were evident clinically.

There are, however, certain specific intracellular changes which command attention. The intranuclear inclusions are similar to those seen in virus diseases, such as herpes simplex, varicella, herpes zoster and virus III disease of rabbits. The intracytoplasmic bodies resemble degenerative products more than specific inclusions.

The changes generally described in the brains of patients who have died of epidemic encephalitis are somewhat similar to those which occur in diseases in which a virus is the known etiologic agent, but no specific cellular changes characteristic of a virus infection were recorded before the report of the first case in this series. The presence of intranuclear inclusions of the type found in these two cases leaves little doubt that a filtrable virus was at least associated with the encephalitis, and since the inclusion bodies are seen in acutely necrotic cells it is probable that they are evidence of the action of a neurotropic virus which caused the encephalitis.

The presence of inclusion bodies in these two isolated cases in which the diagnosis would ordinarily be epidemic encephalitis forces one to speculate as to their significance. If these are typical cases of epidemic encephalitis, similar inclusion bodies should have been described before. It is hardly possible that the sections studied in other cases were not stained in a manner suitable for their demonstration, as they are perhaps best demonstrated in tissues fixed in Zenker's solution and stained with hematoxylin and eosin. The specific inclusions may have been present in small areas which were not sectioned, or they may have been overlooked. In both cases reported here the inclusions were very numerous and conspicuous, and it seems probable that they belong to a different type of encephalitis from those previously studied, which is characterized by the sudden onset of symptoms pointing to cortical involvement, subsequent rapid development of hyperkinetic manifestations and parkinsonism and, after a period of lethargy, high fever and death. The distinguishing pathologic feature is the presence of the intranuclear inclusions within the neurons and neuroglia cells of the brain, which shows, in addition, the general nonspecific changes of acute, subacute and chronic encephalitis. Although there are certain clinical features which seem to indicate that these two cases belong in the same group, it is the presence of the inclusion bodies within the cells which is of primary importance in differentiation.

Because of the confusion which exists in regard to the etiology of the protean disease which at present is called epidemic encephalitis (encephalitis lethargica), it seems wise to subdivide it as early as possible on the basis of a demonstrable differential pathologic lesion. Although

filtrable viruses have been considered as possible etiologic agents, there is little actual evidence that this is true, and there is certainly no proof that a single virus is responsible for the entire group. In the cases reported here there is definite cytologic evidence of virus activity in the form of inclusion bodies typical of virus diseases. Furthermore, there are clinical features which may be of value in differential diagnosis. Because of these facts it seems wise to distinguish this group of cases within the heterogeneous group epidemic encephalitis and give it a specific designation. "Inclusion encephalitis" is probably the most accurate term which could be applied to this group, since it is this feature which is its pathognomonic characteristic.

It is realized that one may err in interpreting the significant features of this small series of cases. Nevertheless, it seems advisable at present to use all available methods in an effort to clarify the picture of epidemic encephalitis. It may be that inclusions will be found in a great number of cases, and it is equally likely that one will find them in a very small percentage. In any event, this specific cytologic lesion will make possible an anatomic subdivision. For this reason it is hoped that careful examination of all available tissues will be made in order to corroborate and add to these observations. The possibility that the cutaneous lesions in the second case may have been an integral part of the picture should be borne in mind, and a careful lookout should be kept for this feature and for other features which may serve to unify or subdivide the group of "inclusion encephalitis."

CONCLUSIONS

1. Because of the presence of intranuclear inclusion bodies within degenerating nerve and glia cells in the cerebral lesions in two cases diagnosed clinically as epidemic encephalitis, it is thought that a virus was responsible for these specific lesions.

2. In view of the negative results following the inoculation of rabbits with emulsions of brain from these patients, one is justified in excluding the virus of herpes simplex as a possible etiologic agent.

3. Because of the pathologic identity and clinical similarity of these two cases of encephalitis, it is suggested that they constitute a new and heretofore unrecognized group of encephalitis.

4. For these reasons it is judged that this group of cases should be distinguished specifically within the heterogeneous group epidemic encephalitis.

5. The noncommittal term "inclusion encephalitis" is suggested as a name for this group.

PECULIAR CONDITION IN CELLS OF EXTERNAL GENICULATE BODY RESEMBLING AMAUROTIC IDIOCY

ALBERT T. STEEGMANN, M.D.
CLEVELAND

A peculiar cellular condition resembling that found in amaurotic idiocy but limited almost exclusively to the external geniculate body has been observed recently by Spielmeyer. I have made a search for such cells in a large number of cases, with the results to be reported in this paper. The condition is a type of pigment atrophy and therefore occurs most frequently in old age. The study involved consideration of the amount of lipoid pigment in nerve cells, a problem originally investigated by Obersteiner [1] in 1903. Curiously, Obersteiner did not include the cells of the external geniculate body in his work.

MATERIAL AND METHODS

Although the external geniculate body is not sectioned as a routine at the Deutsche Forschungsanstalt für Psychiatrie, it was possible to find suitable sections in about one hundred and fifty cases from the collected material. In most cases the sections were from only one side. Specimens from several additional cases were loaned to me by Professor Scholz. The material included a variety of diseases: toxic infectious, sclerotic and other types.

The type of cells to be described was found in ten cases, all occurring in persons over 60 years of age (from 63 to 85½ years). The diagnosis in these cases were: senile changes, one; senile dementia, two; cerebral arteriosclerosis, three; cerebral syphilis, one; diabetes mellitus with coma, one; carbon monoxide poisoning, one, and funicular spinal disease, one.

An estimate of the amount of lipoid pigment in the various cell groups was made. This estimate was based on the average pigment content shown by the Nissl stain in suitably sectioned cells. The fat stain was used as a check in many cases, and other stains were made to study the lipoid reactions.

From the Deutsche Forschungsanstalt für Psychiatrie, Munich, Germany.

1. Obersteiner, H.: Ueber das hellgelbe Pigment in den Nervenzellen und das Vorkommen weiterer fettähnlicher Körper im Centralnervensystem, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **10**:245, 1903.

PIGMENT IN THE EXTERNAL GENICULATE BODY

The structure of the external geniculate body is too well known to require detailed description. The earlier studies of von Monakow,[2] Minkowski,[3] Malone [4] and others have been supplemented in recent years by the work of Henschen,[5] Brouwer,[6] Putnam,[7] Le Gros Clark [8] and Balado and Franke.[9] In a brain sectioned transversely posterior to the optic tracts, the external geniculate body can be seen medially and above the hippocampal gyrus. It is ovoid, lies horizontally, belongs to the metathalamus and varies in shape in human beings (Putnam). Its under surface is hollowed out to receive the fibers of the optic tract; its head axis goes from anterior to posterior, from inside to outside and from above to below. The ventral surface of the ganglion stands in relationship to the pia and forms a part of the roof of Bichat's fold.

Histologically, the ganglion consists of alternating layers of gray and white matter, the ganglion cells being arranged concentrically around a horizontal fifth layer (Balado and Franke). In the middle portion of the ganglion a ventral hilar fold, which also receives blood vessels, divides the layers into a medial and a lateral limb. The cells in the two or three external rows are large and polygonal, with large processes, and are rich in chromatin and pigment (fig. 1, *a*). The other layers consist of small cells, which are half the size of the large cells; these cells are rounded or oval, are densely crowded together and have

2. von Monakow, C.: Experimentelle und pathologisch-anatomische Untersuchungen über die Beziehungen der sogenannten Sehsphäre zu den infracorticalen Opticuszentren und zum Nervus opticus, Arch. f. Psychiat. **14**:669, 1883; **16**:151 and 319, 1885; Gehirnpathologie, Vienna, A. Hölder, 1905, p. 92.

3. Minkowski, M.: Zur Physiologie der Sehsphäre, Arch. f. Anat. u. Physiol. (Physiol. Abt.) **141**:171, 1912.

4. Malone, E.: Ueber die Kerne des menschlichen Diencephalon, Neurol. Centralbl. **29**:290, 1910.

5. Henschen, S. E.: Zur Anatomie der Sehbahn und des Sehzentrums, Arch. f. Ophth. **117**:403, 1926.

6. Brouwer, B.: Experimentelle anatomische Untersuchungen über die Projektion der Retina auf die primären Opticuszentren, Schweiz. Arch. f. Neurol. u. Psychiat. **13**:118, 1923.

7. Putnam, T.: Studies on the Central Visual System: I. The Anatomic Projection of the Retinal Quadrants on the Striate Cortex of the Rabbit, Arch. Neurol. & Psychiat. **16**:1 (July) 1926; II. A Comparative Study of the Form of the Geniculostriate Visual System of Mammals, ibid. **16**:285 (Sept.) 1926: III. The General Relationships Between the External Geniculate Body, Optic Radiations and Visual Cortex in Man, ibid. **16**:566 (Nov.) 1926; IV. The Details of the Organization of the Geniculostriate System in Man, ibid. **16**:683 (Dec.) 1926.

8. Clark, W. E. L.: A Morphological Study of the Lateral Geniculate Body, Brit. J. Ophth. **16**:264, 1932.

9. Balado, M., and Franke, E.: Ueber den Bau des Corpus geniculatum externum des Menschen, Zentralbl. f. d. ges. Neurol. u. Psychiat. **56**:247 and 248, 1930; **62**:710, 1932; **63**:418, 1932.

less distinct processes (fig. 1, *b*). Balado and Franke distinguished three or four types of cells, but the division into a magnocellular and a parvocellular group according to Malone's classification is sufficient for all practical purposes. The arrangement in concentric layers is maintained posteriorly from the hilus, where the ganglion shows an extension of the lateral limb; anteriorly the concentric arrangement, as well as the larger cells, tends to disappear, and the small cells become densely packed together and arranged in sagittal bundles.

The normal cell structure of the external geniculate body in a child, aged 4, is shown in figure 1. In figure 2 are shown the changes in the

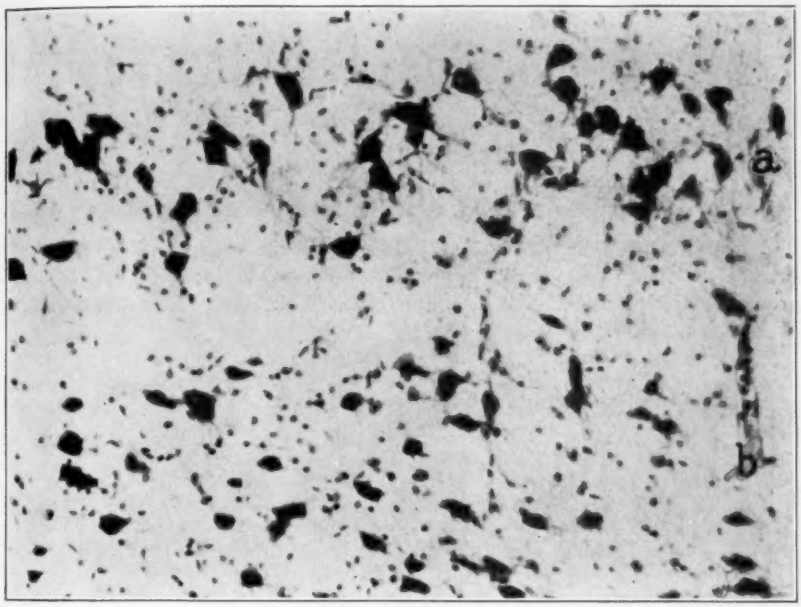

Fig. 1.—Normal cells of the external geniculate body in a child, aged 4 years: *a* indicates the large cell layer; *b*, a part of the small cell layer. Nissl stain; × 180.

cells in the case of a child of the same age with the juvenile form of amaurotic idiocy. All the cells are greatly swollen and loaded with lipoid material lying in a delicate blue reticulum; the nucleus is pushed to the edge of the cell or into the base of a dendrite and in some instances is shrunken, dark-staining and changed in contour; the Nissl granules have disappeared or remain as small rests clustered around the nucleus. In places the cytoplasm is also shrunken and deeply stained, and the remaining bulk of the cell is a large sack of the lipoid-containing constituent. The dendrites are also swollen and laden with pigment.

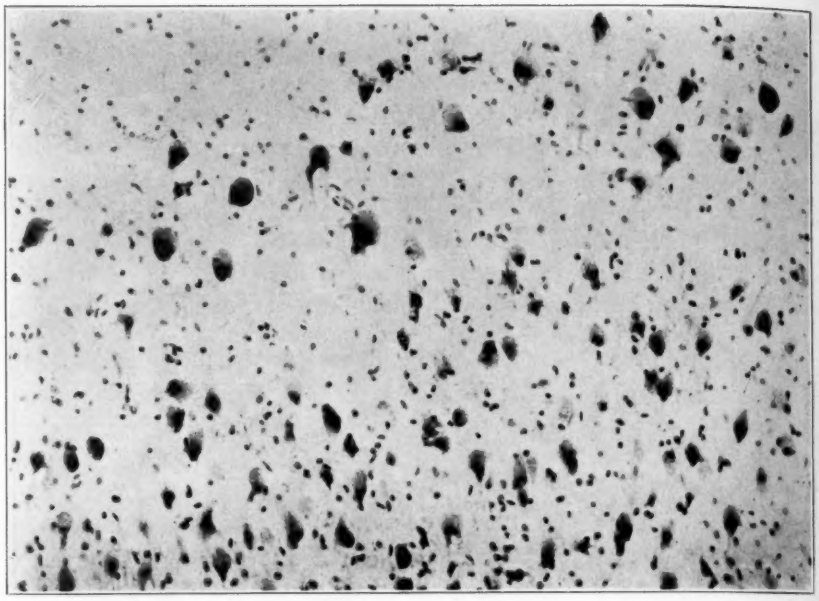

Fig. 2.—Cells of the external geniculate body in a child, aged 4 years, with juvenile amaurotic idiocy. The large cells are seen above; the cell bodies are greatly swollen from the accumulation of lipoid, which lies in a meshlike reticulum. Nissl stain; × 171.

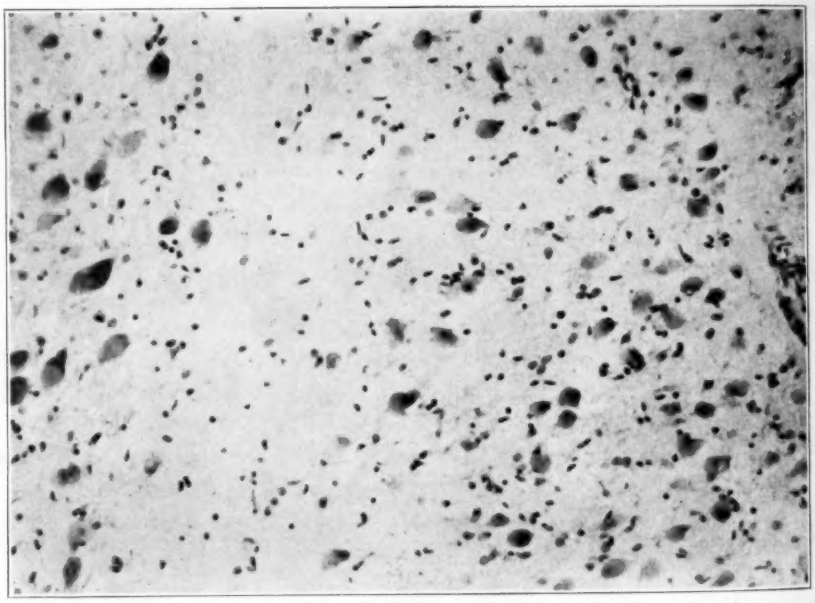

Fig. 3.—Pigment atrophy in the external geniculate body in a senile person. The cells resemble those shown in figure 2. Some of the large cells are seen at the left of the photomicrograph. Nissl stain; × 180.

Figure 3 represents the changes in the external geniculate body in the case of a patient, aged 66, with cerebral arteriosclerosis. Here again all the cells are greatly swollen, with light yellow lipoid pigment, which in some instances stained bluish or greenish with the Nissl stain. Except for the color of the pigment, the morphologic appearance is identical with that of the cells shown in figure 2. Here also the lipoid rests in a delicate blue reticulum (figs. 4 and 5), and the nucleus has been pushed to the periphery of the cell or into the base of a dendrite. Some cells show the change already known to Alzheimer and described as fatty

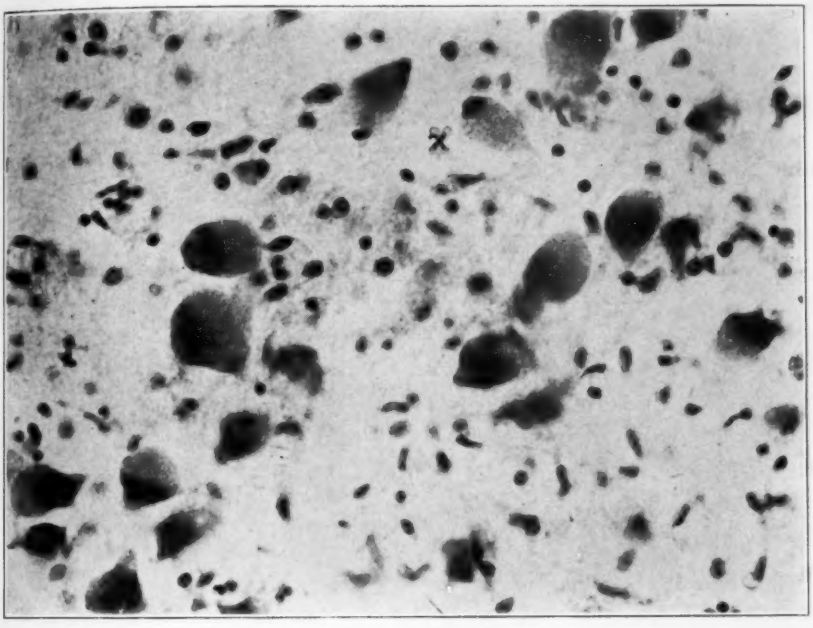

Fig. 4.—Changes similar to those shown in figure 3 in the large cell area of another patient. The cell distortion, the displacement of the nucleus and the lipoid-filled reticulum are visible; *x* indicates a cell undergoing fatty sclerosis. Nissl stain; × 530.

sclerosis (*fettige Sklerose*) or sclerosis with fatty change (*Sklerose mit fettiger Entartung*) by Simchowicz.[10] In such cells (designated by *x* in figures 4 and 5) the nucleus becomes pyknotic and deeply stained. The nucleolus, when visible, may appear very large, and the nucleus may assume an oval or an elongated form. The cytoplasm, apart from the lipoid mass which comprises most of the cell, also tends to shrink,

10. Simchowicz, T.: Histologische Studien über die senile Demenz, in Nissl, Franz, and Alzheimer, Alois: Histologische und histopathologische Arbeiten über die Grosshirnrinde, Jena, Gustav Fischer, 1910, vol. 4, p. 269.

so that in the later stages both the nucleus and the cytosplasm are shrunken into a homogeneous dark blue mass. The rest of the cell is a large, saclike mass of pigment resting in a blue meshlike reticulum. Simchowicz did not mention that the pigment in this process assumes a much more intense yellow color. This is perhaps due to the denser packing together of the pigment granules in the shrinkage process or to the fact that the accumulation of pigment has apparently reached the stage at which degeneration of the cell is the inevitable result. The change in color is best seen when the pigment retains its original yellowish color (*Eigenton*). Simchowicz thought that the fatty change

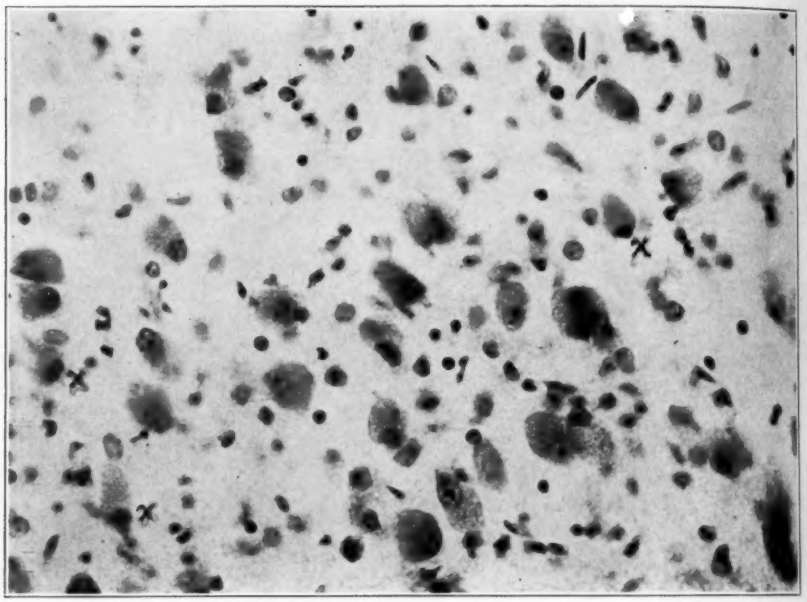

Fig. 5.—The same type of changes as are shown in figure 4 from the small cell area of another patient. The changes in the ganglion cells are the same as those shown in figure 4; *x* indicates cells showing fatty sclerosis. The progressive macroglia cells are easily seen. Nissl stain; × 430.

occurred first, and that on this was engrafted the sclerosis. He believed that such cells do not degenerate as rapidly as cells undergoing simple lipoid pigment degeneration and that they are therefore retained longer in the tissues.

It has been possible to follow the fate of some cells undergoing fatty sclerosis a step farther. In rare instances cells were found in which the shrunken nuclei had become broken up into coarse dark granules. These granules had separated and either spread out in the cell itself or migrated into the surrounding tissues. This process of degeneration by

karyorrhexis is analogous to a similar type of degeneration seen in regressive glia cells.

Swelling of the dendrites was not so pronounced as in the case of amaurotic idiocy used for comparison, but was seen occasionally and is probably normal for the cells of the external geniculate body in old age. An example is shown in figure 6.

With the Nissl stain the pigment granules sometimes occupy only a part of the space in the reticulum, other lipoid constituents being removed by the lipoid solvents in the process of embedding. When the

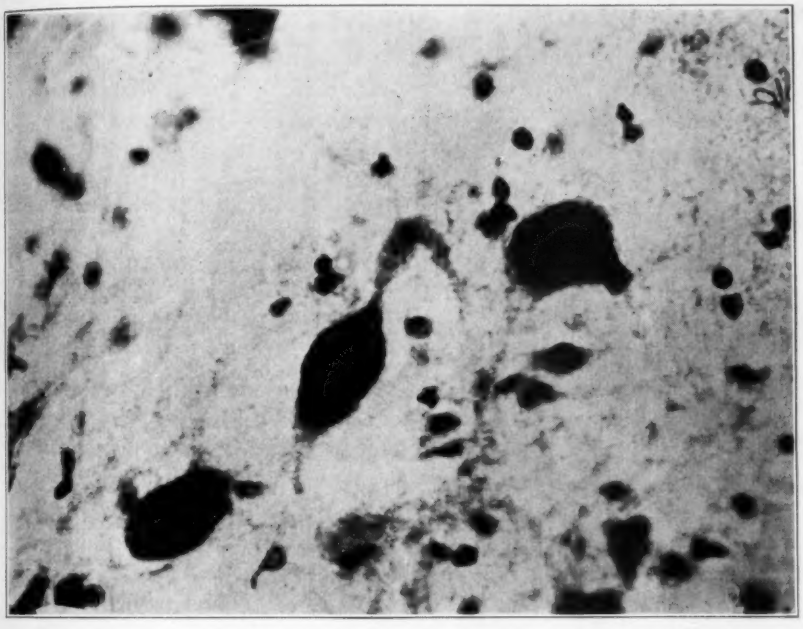

Fig. 6.—A swollen dendrite filled with pigment. Nissl stain; × 680.

cells are examined with a fat stain a larger amount of lipoid often takes the fat stain than can be seen with the Nissl stain. In some cells this disproportion between the two stains is evident.

Other staining methods revealed nothing new, and their effects on lipoid pigment are well known. The Bielschowsky method stained the reticulum dark brown and showed the nodal points of the reticulum clearly. The pigment granules did not stain with the Spielmeyer stain for myelin sheaths. With the Smith-Dietrich method the granules stained dark gray with sparse black stipples. Only sparse black granules could be seen with the Heidenhain stain. The granules stained blue with the Alzheimer-Mann method and greenish blue with nile blue sulphate.

The glia cells showed no remarkable changes, considering the age of the patients. Cells with large, round, clear, delicately stippled nuclei and scanty cytoplasmic processes are apparently normal in the external geniculate body, especially in old age. Somewhat similar glia cells, which, however, are denser and have nuclei more irregular in contour, occur in the olive and in the dentate nucleus of the cerebellum and are considered normal by Scherer.[11]

In some cases, however, there were definite progressive reactions of the fixed glial elements, especially the macroglia. Rod cells were seen only rarely. Such changes are regular in senility according to Simchowicz.[10] Pigment granules were seen in both the progressive and the regressive macroglia cells. Some of the regressive forms with dark, irregular, pyknotic nuclei contained much pigment, which assumed a more intense yellow color, as in fatty sclerosis of the ganglion cells. It is interesting that in some cases the glia cells were almost free from pigment, whereas the ganglion cells showed a most striking pigment atrophy, as already described.

In the cases in which there was no underlying vascular disease due to such a condition as arteriosclerosis or syphilis, the only changes found in the blood vessels were those associated with senility. These include pigment in the endothelial cells, which were pyknotic or sometimes swollen, and a slight increase of the adventitial cells, with or without pigment.

The condition of the ganglion cells under study, which histopathologically may be described as pseudo-amaurotic idiocy, occurred only in the external geniculate body, with the exception of one case in which there were similar changes in the amygdaloid nucleus. In this case there were also ganglion cells which presented the homogeneous type of nuclear degeneration typical of Pick's atrophy. In one case the cellular changes in the external geniculate body were associated with phenomena of degeneration. In this case, in a part of the last layer of small cells there was a partial *Ausfall,* and the remaining cells, although smaller than the cells in the undegenerated area, were very rich in pigment. Fatty sclerosis was also prominent, suggesting that Simchowicz was probably right when he said that such cells are retained longer in the tissues than cells undergoing ordinary pigment atrophy. There was a corresponding increase in the fixed glia cells. The ganglion cells in the undegenerated area were also rich in pigment.

In amaurotic idiocy the cells of the external geniculate body are not necessarily changed in the manner described. A case studied by

11. Scherer, H. J.: Beiträge zur pathologischen Anatomie des Kleinhirns, Ztschr. f. d. ges. Neurol. u. Psychiat. **139**:337, 1932.

Spielmeyer,[12] with most pronounced cell changes in the spinal cord, showed few changes in the external geniculate body.

In rare instances the amount of pigment in old age may not be excessive. As a rule, however, the accumulation of pigment in old age is pronounced, and this raises the question of the amount of pigment in the cells of the external geniculate body as compared with other cell groups of the central nervous system. A comparison of the pigment content of various cell groups was made in the cases of persons of different ages. With the Nissl stain, no pigment was found in the external geniculate body in children of 8 years, but in children in early adolescence, about 12 years of age, small scattered granules of pigment were seen resting among the Nissl granules. At this age the cells of the thalamus contained more pigment than those of the external geniculate body, but no pigment was detected in the cells of the olive or the dentate nucleus, the Betz cells or the motor cells of the medulla or midbrain. After the age of 18 or 20, the pigment is well established and rests, as a rule, in a reticulum at the edge of the cell or against one or more dendrites. Unlike the melanin pigment, therefore, the lipoid pigment tends to accumulate gradually with age, varying widely in certain cell groups and in different persons.

Of the larger cells of the nervous system, the cells of the olive, the dentate nucleus and the nucleus magnocellularis thalami and the large pyramidal cells contain the most pigment. In the cortex, the pyramidal cells of the frontal and temporal lobes, the cells of the cornu ammonis and a group of large pyramidal cells at the beginning of the subiculum, which encroach on the molecular layer, have the most pigment. The last cells were first described by Hulst and are among the richest in pigment content of the cortical cells, according to Obersteiner.[1]

It is also to be noted that a number of smaller cells in the brain are very rich in pigment. These include the pyramidal cells of the outer and inner granular layers of the cortex (Simchowicz), the cells of the nucleus parvocellularis thalami (Malone) and certain small and medium-sized cells of the pontile region in the median raphe and around the aqueduct (Obersteiner). Similar cells can also be seen in the median raphe of the medulla. The pigment of such cells does not rest in a reticulum as a general rule; instead, the granules are scattered or packed throughout the cell cytoplasm. It is naturally difficult to compare the pigment content of such cells with that of the large nerve cells.

In old age it was found that among the larger nerve cells the cells of the olive consistently contain the largest amount of pigment. The cells of the external geniculate body are second in the degree and con-

12. Spielmeyer, W.: Family Amaurotic Idiocy, in Henke, F., and Lubarsch, O.: Handbuch der speziellen pathologische Anatomie und Histologie, Berlin, Julius Springer, to be published.

sistency of storage of pigment. The cells of the dentate nucleus and the large cells of the thalamus show considerable variation in the amount of pigment, both individually and as a group, and only rarely compare with those of the external geniculate body. The same is true of the cells of the cornu ammonis, the amygdaloid nucleus, Meynert's ganglion and the cortex.

COMMENT

The cells of the external geniculate body are strongly lipophilic and begin to store pigment in early adolescence. One can only conjecture that the cellular changes which I have described in the external geniculate body depend on the pronounced tendency of these cells to lipoid change, which occasionally reaches the pathologic proportions found in these ten cases. Although pronounced pigment atrophy may be associated with cell defects (*Ausfälle*), the pigment change probably represents a mode of reaction of the cell to such injuries, because in most of the cases it was present where no such cellular defects existed. In the arteriosclerotic cases no direct relationship was found between the degree of arteriosclerosis and the degree of pigment change, nor were the cells in areas showing severe ischemic changes shown to contain more pigment.

Although many theories have been advanced, the origin of this pigment is obscure, and studies in microchemistry and metabolic chemistry have not solved the problem, as Obersteiner hoped they would. The pigment is highly resistant to fat or lipoid solvents; probably, when once formed in the cell, it cannot be changed by the cell metabolism and thus be eliminated. Marinesco [13] linked the pigment with the process of cell involution, and Lubarsch [14] called it a "wear and tear" (*Abnutzung*) product. Mühlmann [15] explained its origin by a lack of nutrition of the cell, either from toxic causes or from actual limitation of the amount of nutrition. Hueck [16] called the pigment *Lipofuszin,* and separated it from lipochrome pigment because the latter does not occur in relation with a fatlike substance. Hueck thought that the pigment is a degeneration product of fatlike substances, such as phosphatides and cerebrosides, with which it is bound chemically.

The relationship of ordinary lipoid pigment to the lipoid found in the cells in amaurotic idiocy is interesting in the light of Hueck's work.

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13. Marinesco, G.: La cellule nerveuse, Paris, O. Doin, 1909, p. 283.

14. Lubarsch, O., cited by Oberndorfer, S.: Die pathologischen Pigmente, Ergebn. d. allg. Path. u. path. Anat. **19**:117, 1921.

15. Mühlmann, M.: Untersuchungen über das lipoide Pigment der Nervenzellen, Virchows Arch. f. path. Anat. **202**:153, 1910.

16. Hueck, W.: Pigmenstudien, Beitr. z. path. Anat. u. z. allg. Path. **54**:68, 1912.

When Spielmeyer [17] first described the juvenile type of amaurotic family idiocy, he not only mentioned that the lipoid had a yellowish-green color (with the Nissl stain) but expressed the opinion that it stood in relationship to ordinary lipoid pigment in some way. In the later forms of amaurotic idiocy, described by Kufs,[18] the lipoid also has a yellowish color, and the disease is less universal, involving certain cell groups more than others. For example, in the "latest" form described by Kufs the cells of the cornu ammonis, the substantia nigra and the olive were most involved. The lipoid of the late forms of amaurotic idiocy not only approaches the lipoid pigment in appearance but shows a tendency in the same direction chemically. In fact, Hurst [19] and more recently Grinker [20] investigated these chemical reactions and agreed with Schaffer [21] that the acuteness of the process in the infantile form as compared to the chronicity of the process in the juvenile and later forms determines the staining reactions of the lipoid. The acute process in the infantile form liberates soluble cerebrosides and phosphatides, but when the disease has a more chronic course more insoluble lipoids are liberated, gradually approaching nearer to lipoid pigment.

The studies of metabolic products in senility present many problems that are no less interesting than those concerned with pathologic metabolites in amaurotic idiocy, which is now considered by many investigators [12] to be a form of the Niemann-Pick disease. In fact, the future may prove these metabolic products to have analogous features of which there is only a hint at present.

CONCLUSIONS

1. The cells of the external geniculate body are among those richest in lipoid pigment in the central nervous system.

17. Spielmeyer, W.: Klinische und anatomische Untersuchungen über eine besondere Form von familiärer amaurotischer Idiotie, Gotha, Engelhard-Reyher, 1907.

18. Kufs, H.: Ueber eine Spätform der amaurotischen Idiotie und ihre heredofamiliären Grundlagen, Ztschr. f. d. ges. Neurol. u. Psychiat. **95**:169, 1925; Ueber einen Fall von Spätform der amaurotischen Idiotie mit atypischen Verlauf und mit terminalen schweren Störungen des Fettstoffwechsels im Gesamtorganismus, ibid. **122**:395, 1929; Ueber einen Fall von spätester Form der amaurotischen Idiotie mit dem Beginn im 42. und Tod im 59. Lebensjahre in klinischer, histologischer und vererbungs-pathologischer Beziehung, ibid. **137**:432, 1931.

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2. These cells, which begin to accumulate lipoid pigment in adolescence, may occasionally in old age show a pronounced pigment atrophy which makes the morphologic appearance of the cells resemble the changes produced by amaurotic family idiocy. The chief difference is in the nature of the lipoid substances.

3. Because this peculiar cellular picture is limited to the external geniculate body, there is no difficulty in making a differential diagnosis between this process and that of family amaurotic idiocy, in which the extension of the Schaffer-Spielmeyer cell process is universal.

PARASELLAR TUMORS

MENINGEAL FIBROBLASTOMAS ARISING FROM THE SPHENOID RIDGE

BERNARD J. ALPERS, M.D.
AND
ROBERT A. GROFF, M.D.
PHILADELPHIA

Within recent years there has been considerable clarification of knowledge of lesions in and around the sella turcica, particularly of tumors in this area. The characteristics of intrasellar and suprasellar tumors have been so clearly portrayed that much that was completely obscure has now been effectively clarified. There still remain some lesions about the sella turcica concerning which knowledge is not entirely clear, however. Among them is a group of tumors which arise from the sphenoid ridge, which occupy a position near or beside the sella turcica, and which may therefore be reckoned among the parasellar tumors. It is these which we shall attempt to analyze, with the hope of indicating some characteristics that are common to the group.

MATERIAL

Strictly speaking, the parasellar tumors include all tumors near or beside the sella turcica. This would include tumors not only in relation to the wings of the sphenoid bones, but also those situated in the middle fossa. The latter have been subjected to study in this clinic,[1] so that we shall confine our remarks to tumors that bear an intimate relationship to the wings of the sphenoid bone, or the so-called tumors of the sphenoid ridge. There are eight examples of this type of tumor in Dr. Frazier's group of verified tumors, exclusive of tumors which have arisen elsewhere and have extended into the parasellar area. Intrasellar tumors which spread into the parasellar region have not been included in the group.

The cases we present vary in clinical manifestations because of differences in size and location. Those lying medially on the sphenoid ridge, on the lesser wing, have manifestations different from those lying laterally on the greater sphenoid wing.

From the Neurosurgical Wards of Dr. C. H. Frazier and the Laboratory of Neurosurgery in the Hospital of the University of Pennsylvania.

The expenses of this investigation were defrayed by the Charles Harrison Frazier and the Frances Clark Funds for Neurosurgery.

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THE LESSER WING GROUP

CASE 1.—*Small tumor of the right sphenoid ridge arising from the lesser wing, with symptoms of less than six months' duration. No change in the fundi; visual acuity, right eye, 6/9; left eye, 6/4; incomplete left homonymous hemianopia. Complete paralysis of the right third nerve with loss of pupillary reactions. Spinal*

Fig. 1 (case 1).—Complete oculomotor paralysis of the right side.

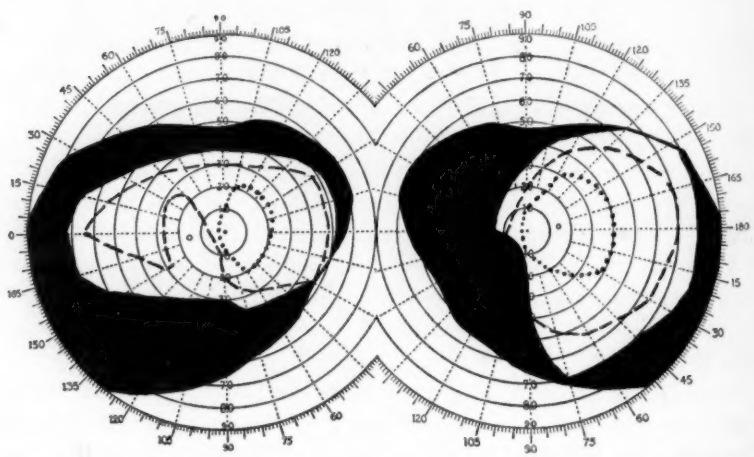

Fig. 2 (case 1).—Homonymous hemianopia with a marked inferior quadrantic cut in the temporal field of the left eye.

fluid pressure, 140 mm. of water. Sella turcica, "top normal" in size. Encroachment on the right lateral ventricle from the side and below, seen by ventriculography. Partial removal of fibroblastoma attached to the dura.

History.—W. B., a man, aged 36, who was referred to the service of Dr. C. H. Frazier in the University Hospital by Dr. C. H. Humes, of Indianapolis, had been well until six months before entrance, when he noticed diplopia on the right while

bending over. Following this the diplopia was constant and in both lateral directions. At this time also he observed slight impairment of vision. He continued in this state until three months before entrance, when there developed severe right frontal headaches, which were entirely nocturnal. Following this there appeared sharp, shooting pains on the right side of the head, which were aggravated by movements of the head. Three weeks before admission to the hospital, he noticed drooping of the right eyelid, a condition which progressed to complete ptosis within three weeks.

Examination.—The neurologic findings were confined to the eyes. There was complete external and internal ophthalmoplegia of the right eye, with ptosis, paralysis of the right eyeball upward, inward and downward, and loss of the pupillary reactions, both to light and in accommodation (fig. 1). There was at first no evidence of optic atrophy or papilledema. Later examination showed slight bilateral optic atrophy. The visual fields, however, showed an incomplete left homonymous hemianopia, with an inferior temporal quadrantic cut in the left temporal and right

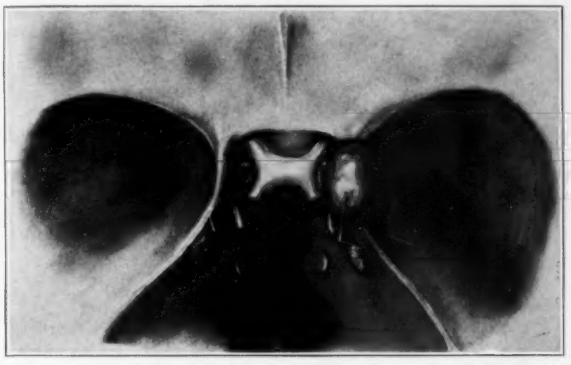

Fig. 3 (case 1).—A small tumor of the lesser wing compressing the oculomotor nerve, the optic tract and the internal carotid artery.

nasal fields, and a cut not so complete in the right superior nasal quadrant (fig. 2). There was no evidence of increased intracranial pressure, the manometric reading being 140 mm. of water. A roentgenogram of the sella turcica showed no increase in size, the measurements being 12 by 11 mm. The dorsum seemed to be rarefied rather than atrophic, and there was marked calcification of the portion of the dura along the clavus.

Ventriculographic studies showed an encroachment on the right lateral ventricle from below and laterally. The rest of the ventricular system was intact. Encephalographic studies showed the third ventricle deviated slightly to the left.

Operation.—On March 4, 1931, Dr. F. C. Grant elevated a right temporoparietal bone flap, exposing a small fibroblastoma arising from the sphenoid ridge and extending into the middle fossa (fig. 3). The tumor appeared as a bluish cyst at the most mesial portion of the lesser sphenoid wing, close to the internal carotid artery. The cyst was evacuated and part of the wall removed.

Pathologic Changes.—The tumor was encapsulated. It was very cellular, the cells being arranged in groups. Around each group of cells was a thin connective tissue structure. The tumor was very vascular. The cells were flat and large, with large vesicular nuclei. The tumor was difficult to classify. Its great vascu-

larity and the large flat cells, which were different from those of the usual meningeal fibroblastoma, were confusing. It was classified finally as a meningeal fibroblastoma of very vascular type.

Comment.—There were few findings in this case, and for this reason diagnosis was difficult. The most suggestive factors were the homonymous hemianopia and the evidence of complete paralysis of the right third nerve. The optic nerves showed neither atrophy nor edema. The roentgen findings were inconclusive. The case might have been discarded merely as one of suspected tumor of the brain were it not for the visual fields, but in order accurately to localize the lesion a ventriculogram was necessary. As this was inconclusive, encephalography was performed. This, too, was not definite. There were sufficient signs in the ventriculogram to suggest the presence of a tumor, however, and a craniotomy was performed.

The operative findings explain adequately the clinical features of the case. The tumor lay on the sphenoid ridge close to the internal carotid vessel, which it compressed, extending to the right oculomotor nerve, which was also compressed. The changes in the visual field could have been caused either by direct compression of the optic tract laterally or by pressure against the internal carotid artery, which could have been pushed backward and produced a notching of the right optic tract. The latter seems the more likely in view of the position of the tumor and the location of the internal carotid vessel normally in relation to the optic chiasm and tracts. Of particular interest is the absence of any changes in the optic nerve itself.

The case represents an early type of tumor of the sphenoid ridge, causing only localized symptoms and no increase in intracranial pressure. It lay in close relation to the anterior clinoid process of the right side, and to the side of the sella turcica.

The second case is also one of a small tumor which arose from the lesser sphenoid wing. It illustrates further the intimate relationship between these tumors and the structures close to the lesser sphenoid wing.

CASE 2.—*Small tumor of the left sphenoid ridge arising from the lesser wing. Progressive symptoms for one year. Bilateral primary optic atrophy. Visual acuity, 20/200 in both eyes. Right homonymous hemianopia. Slight right facial weakness. Impairment of taste. Weakness of the right hand. Basal metabolic rate, —12. Normal intracranial pressure. Pointing of the anterior clinoid processes and possibly some atrophy of the dorsum sellae. Sella turcica "top normal" in size, 12 by 6 mm. Incomplete removal of the tumor at operation.*

History.—J. F., a man, aged 37, who was referred by Dr. B. F. Baer, of Philadelphia, to the service of Dr. C. H. Frazier in the University Hospital, one year before entrance had noticed impairment of vision. Vision continued to fail, but he was able to work until two weeks before entrance to the hospital. Coincident with the visual disturbances he had fleeting pains in the head. These headaches were

generalized, occurred about every three days and showed no tendency to increase in frequency or severity. During the onset of the symptoms, he had noticed decreased sexual desire. This had progressed to complete loss at the time of admission.

Examination.—There was bilateral primary optic atrophy, with markedly decreased visual acuity, measuring 20/200 in both eyes. Studies of the visual

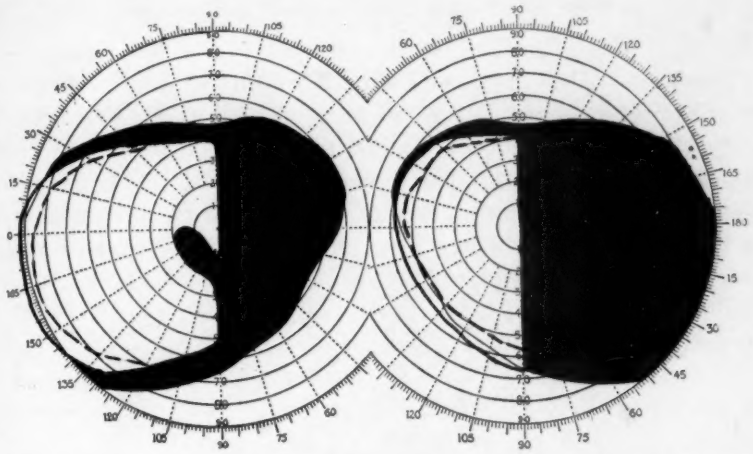

Fig. 4 (case 2).—Homonymous hemianopia extending through the fixation point.

Fig. 5 (case 2).—A small tumor of the lesser wing in intimate contact with the optic nerve, chiasm and tract and the anterior cerebral vessel.

fields revealed a clearcut left homonymous hemianopia (fig. 4). Examination of the cranial nerves gave negative results otherwise. There were slight central facial weakness on the right, slight weakness of the right arm and hand, the grip being 45 as compared with 60 on the left, and slight increase in the right biceps reflex. There was no involvement of the leg. Endocrine disturbances, though not conspicuous, were present. They consisted of complete loss of libido, polyuria, a rather pronounced gain in weight in the year previous to admission, slight loss of hair, smooth and silky skin and somnolence.

Operation (Dr. F. C. Grant).—A tumor of the left sphenoid ridge was exposed through a large frontotemporal bone flap. The tumor lay beneath the left optic nerve, between it and the left anterior cerebral artery (fig. 5). The left optic nerve coursed over the median pole of the tumor, which lay on the sphenoid ridge, just lateral to and involving the left anterior clinoid process. The tumor was removed only in part because of its close relation to the anterior cerebral artery.

Pathologic Changes.—The pathologic structure was similar to that in the preceding case. Histologically the tumor was diagnosed as a vascular type of meningeal fibroblastoma.

Comment.—This was a medially placed tumor, which compressed the left optic nerve and was intimately related to the left anterior cerebral artery. It produced bilateral primary optic atrophy and right homonymous hemianopia. The motor symptoms of weakness of the right side of the face and right hand are a little difficult to explain on the basis of a basilar tumor. They may conceivably have been due to compression and temporary occlusion of a band of the left middle cerebral vessel. Despite the intimate relation to the sella turcica, there was nothing particularly suggestive in the sellar changes.

In the two following cases the signs are more extensive because of the greater size of the tumor, the sellar changes being particularly striking.

CASE 3.—*Tumor of the right sphenoid ridge. Progressive loss of vision for four years. Optic atrophy of the right eye and papilledema of the left. Blindness on the right, and inferior left temporal quadrantic cut in the visual field. Loss of sense of smell on the right, but otherwise no neurologic findings. Increased intracranial pressure to 23 mm. of mercury. Complete erosion of the posterior clinoid processes and the dorsum sellae. Operation and partial removal of fibroblastoma of the sphenoid ridge.*

History.—M. S., a woman, aged 32, who was referred to Dr. F. C. Grant by Dr. Luther Peter, with the presumptive diagnosis of a suprasellar tumor, for four years had noticed gradual failure of vision, affecting first the right eye and then the left. The right eye had been blind for almost four years when she was first seen. There had been progressive loss of vision in the left eye for two years before admission to the hospital, with a particularly rapid decline during the two weeks before entrance. She had had no other symptoms, except an external strabismus which she had had since childhood and which was much improved by glasses. There were no symptoms indicative of increased pressure within the skull. There were no outspoken endocrine symptoms, but she stated that she had gained 14 pounds (6.4 Kg.) in two years, and that the menstrual periods were shorter and scanty, while still retaining their regularity.

Examination.—There was a loss of the sense of smell on the right side. The ocular findings constituted the outstanding feature, with optic atrophy of the right eye and choked disk in the left eye. No visual field was present on the right; on the left there was a definite inferior quadrantic cut in the temporal field, with a large notch extending up into the upper quadrant. The basal metabolic rate was —17.

Roentgen examination of the region of the sella turcica showed complete erosion of the posterior clinoid processes and the dorsum sellae. The floor of the sella turcica was thin and encroached markedly on the sphenoid sinus. The sella turcica itself was not enlarged. The sinuses showed no roentgen evidence of disease.

Operation.—On Nov. 16, 1931, Dr. F. C. Grant performed a right transfrontal craniotomy. Elevation of the right frontal lobe revealed a large vascular fibroblastoma arising from the lesser wing of the sphenoid and extending into the anterior and middle fossae by straddling the sphenoid bone. The right optic nerve was completely embedded in the tumor; the left was free (fig. 6). Half of the tumor was removed at this operation.

Pathologic Changes.—The tumor was a typical meningeal fibroblastoma, with psammoma formation.

Comment.—There were rather difficult problems in localization raised by this case. It seemed apparent that there was a tumor in the region

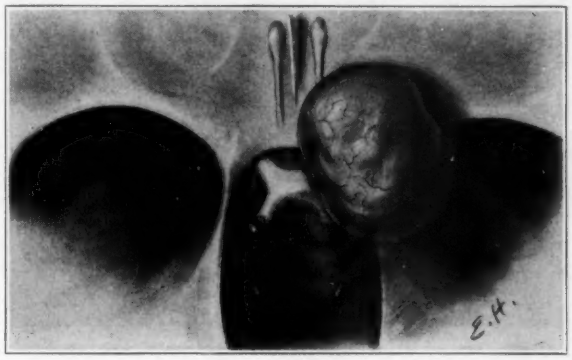

Fig. 6 (case 3).—A large tumor of the lesser wing compressing the right olfactory and optic nerves and the right optic tract.

of the chiasm, but it was not wholly clear where it was located. The visual findings were not characteristic of a suprasellar tumor, because instead of the optic atrophy usual in these cases there was primary atrophy in one eye and papilledema in the other. Furthermore, the degree of increased pressure was much higher than in the usual suprasellar tumor. There seemed sufficient reason to suspect, therefore, that the tumor was not typically suprasellar, though it probably was situated in the chiasmal and sellar area. The roentgen findings, on the other hand, were compatible with a suprasellar tumor.

Essentially, the case was characterized by progressive loss of vision for four years, by papilledema and optic atrophy, by a temporal field cut in the left eye, the only eye in which studies of the fields could be made, by loss of the sense of smell on the right, by evidence of erosion of the sella turcica and by vague menstrual disorders.

At operation, a tumor was exposed which straddled the sphenoid ridge, extending into both the anterior and the middle fossae, com-

pressing the right optic nerve and having some suprasellar extension; the latter was not marked.

This case illustrates a fairly advanced instance of tumor of the sphenoid ridge. Unlike the tumors in cases 1 and 2, it had extended far beyond the sphenoid ridge. Its medial extension at the medial border of the lesser wing of the sphenoid implicated the right optic nerve, while its anterior extension involved the olfactory nerve on the same side. The changes in the visual field are attributable to the lateral compression of the optic chiasm and tract.

CASE 4.—*Tumor of the right sphenoid ridge involving the lesser wing. Progressive loss of vision for five years. Bilateral primary optic atrophy. Right homonymous hemianopia. Visual acuity: right eye, 1/40; left eye, 2/40. Sense of smell impaired on the right. Pituitary fossa 12 by 11 mm. A thin shadow seen about the pituitary fossa. Operation and partial removal of a tumor of the right sphenoid ridge.*

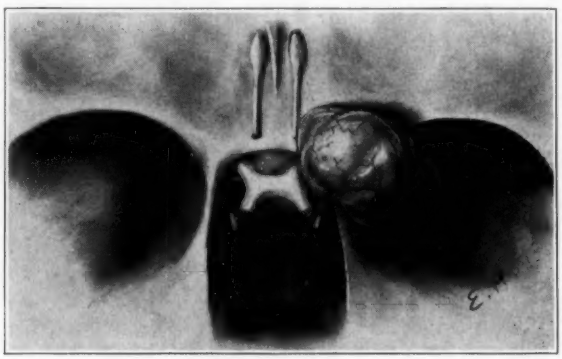

Fig. 7 (case 4).—A large tumor of the lesser wing compressing the olfactory nerve, the optic nerve and the chiasm of one side.

History.—C. M., a woman, aged 66, who was referred to Dr. C. H. Frazier by Dr. H. F. Moffitt, of Altoona, Pa., with the presumptive diagnosis of a tumor of the brain, had been well until five years before admission to the hospital. At about that time she noticed that she could not see as well to the left as formerly. This difficulty progressed until she was unable to see anything to the left of her. Eight months before entrance to the hospital she had suffered an attack of dizziness, with nausea and projectile vomiting. A similar attack had occurred four months later. Within a period of three months before entrance to the hospital, vision had failed to the extent that she was able only to recognize people to the right. Occasionally she had experienced flashes of light.

Examination.—There was bilateral primary optic atrophy. Visual acuity was 1/40 on the right and 2/40 on the left. The visual fields revealed a complete left homonymous hemianopia. Memory was impaired. The sense of smell was decreased on the right. Roentgenograms of the head showed a thin curved shadow about the pituitary body. The pituitary fossa measured 12 by 11 mm., as seen in the roentgenogram.

Operation.—On March 27, 1931, Dr. Frazier performed a right transfrontal craniotomy. When the right frontal lobe was elevated, a tumor was found on the lesser wing of the sphenoid bone, extending backward into the middle fossa (fig. 7). Only partial removal of the tumor was possible.

Comment.—This case resembled the others in this group. The subjective complaint of progressive loss of vision was again in evidence. There were primary optic atrophy and left homonymous hemianopia due to compression of the optic tract by the tumor. The anosmia on the right side was due to extension forward of the tumor, catching the right olfactory nerve. As in many of the other cases, the pituitary fossa was what is described as "top normal" in size.

The next case illustrates the difficulty in diagnosing a small tumor at the extreme lateral extremity of the greater sphenoid wing. Neurologic signs were inconclusive, so that ventriculography was necessary. In contrast to the first four patients, one of whom had normal fundi and three primary optic atrophy, this patient had papilledema of a low degree.

THE GREATER WING GROUP

CASE 5.—*Small tumor arising from the greater wing of the right sphenoid bone. Symptoms for two years, with a free interval of twenty months. Papilledema of 1.5 diopters in both eyes. Vision 6/45 in both eyes. Incoordination of gait. Dysmetria of the left arm. Positive Romberg sign. Spinal fluid pressure, 375 mm. of water. Roentgenogram showed no abnormalities (sella turcica, 9 by 9 mm.). Practically complete obliteration of the right lateral ventricle and pressure defect in the midportion of the left lateral ventricle as seen by ventriculograph. Operative removal of a small meningeal fibroblastoma of the sphenoid ridge.*

History.—M. B., a man, aged 55, who was referred to the service of Dr. C. H. Frazier in the University Hospital by Dr. D. Barsky, of Philadelphia, gave a long history which was involved and confusing. In July, 1929, he entered the University Hospital complaining of dizziness and hyperacusis on the right side. He had been well until May, 1929, about eight weeks before entrance, when he began to suffer from vertigo, buzzing in the ears and hyperacusis affecting both ears, but more particularly the left. These attacks appeared two or three times a day, and were precipitated by sudden turning of the head. Examination at this time showed only papilledma of 5 diopters in both eyes, and a spinal fluid pressure of 250 mm. of water. There were no neurologic signs of significance, but roentgenograms showed infection in both frontal, the left ethmoid and the left maxillary sinuses. He was discharged without operation as suspected of having a tumor of the brain. The vertigo and hyperacusis disappeared after treatment applied to the right ear.

The patient returned in May, 1931, with further symptoms. For two months he had had weakness of the legs and unsteadiness in gait. The dizziness noted on the previous admission was not present. For two weeks before entrance he had suffered from frontal headaches, which were relieved by salicylates. He entered the hospital on this occasion chiefly because of difficulty in walking.

For the two years between his first admission and the present one he had been perfectly well, a fact which made matters even more confusing in diagnosis and localization.

Examination.—A neurologic survey revealed positive ocular findings and some rather confusing signs, which indicated the presence of ataxia of the left arm and

leg. There was bilateral papilledema of 1.5 diopters. The visual acuity was 6/45 in both eyes. The visual fields could not be studied because of the patient's confusion. There were ataxia of the left arm, ataxic gait and a tendency to fall to the left in the Romberg position. The reflexes in the arms were diminished; those in the legs were absent. The cerebrospinal fluid pressure was 375 mm. of water. The pineal gland was visualized by roentgenograms, but no shift was apparent. There was no enlargement of the sella turcica, which measured 9 by 9 mm.

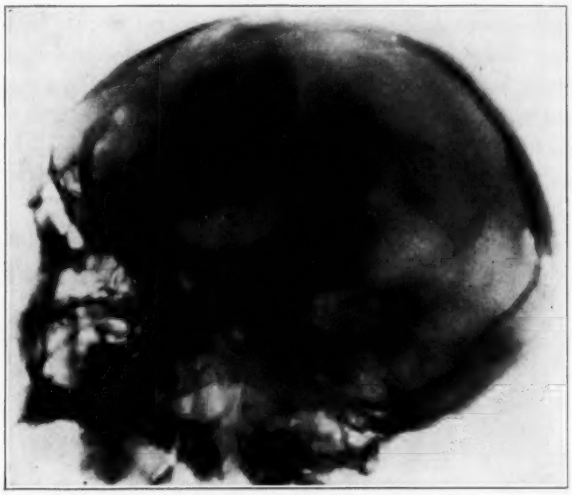

Fig. 8 (case 5).—Ventriculogram, showing obliteration of the atrium of the lateral ventricle.

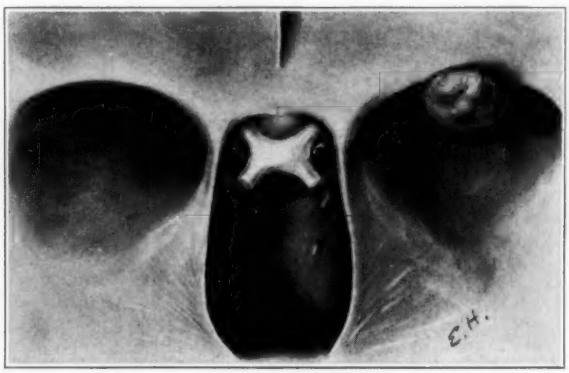

Fig. 9 (case 5).—A small tumor of the greater wing with very few localizing signs.

Ventriculography.—Because of difficulties in localization, ventriculography was performed. The ventriculogram showed absence of air in the body of the right lateral ventricle, with dilated anterior and posterior horns on this side (fig. 8). The left lateral and third ventricles were normal.

Operation.—On June 5, 1931, Dr. Frazier elevated a frontotemporal bone flap under local anesthesia. The temporal lobe was uncapped, and a small tumor aris-

ing from the greater wing of the sphenoid bone was removed. It extended into the middle fossa, chiefly under the temporal lobe, but was definitely attached to the wing of the sphenoid bone (fig. 9).

Pathologic Changes.—Histologic study revealed a well encapsulated tumor, with a dense stroma penetrating into the tumor from the capsule and a fine reticulum around the tumor cells. There were many blood vessels from which new vessels could be seen developing. The cells were endotheliomatous. Fibroglia was not found in the tumor. The tumor appeared to be a vascular type of meningeal fibroblastoma.

Comment.—This case represents an early lesion of the sort under discussion. The history was confusing from the beginning and probably had little to do with the position of the tumor. The only positive findings were papilledema and decreased visual acuity. Because of the mental confusion no examinations of the visual fields were possible.

The tumor sprang from the greater wing of the sphenoid bone, extended into the middle fossa and compressed the inferior and lateral parts of the temporal lobe. It produced few signs which were helpful in diagnosis, chiefly because it was situated in a relatively silent area of the brain. Possibly its small size had something to do with the few symptoms elicited. It was a very small tumor, one of the smallest in the series.

That the tumors in this area are not always confined to a limited portion of the sphenoid ridge is illustrated by case 6, in which the tumor lay in contact with both the lesser and the greater sphenoid wings.

CASE 6.—*Large tumor of the right sphenoid ridge, involving the entire ridge. Progressive symptoms for ten years. Secondary atrophy of the left optic disk; 1 diopter of choking of the right. Visual acuity: left eye, 6/9; right eye, blind. Left field full, with enlarged blind spot in the right field. Spinal fluid pressure 300 mm. of water. Calcified mass over the greater and lesser wings of the sphenoid bone on the right. Operation and partial removal of a tumor on the right.*

History.—C. M., a woman, aged 28, who was referred to the service of Dr. C. H. Frazier by Dr. R. F. Leinback, of Charlotte, N. C., and by Dr. W. G. Spiller, of Philadelphia, ten years previously, while undergoing an examination of the eyes, was found to have almost complete loss of vision for form and color in the right eye. She herself had not recognized this disability. During succeeding years she noticed slight but gradual loss of vision in the left eye. No further symptoms appeared until three years before entrance when, following the birth of a child, she suddenly realized that she could not see out of the temporal half of the left eye. This lasted for about fifteen minutes. One year later, or two years before admission, severe headaches developed. One year before entrance to the hospital, she experienced the first attack of headache and dizziness, which was followed by a sensation of numbness starting in the left side of the face and quickly spreading down the arm and body on the left side. The attack lasted for from ten to fifteen minutes. She did not lose consciousness. Following this she had numerous attacks. These increased in frequency. Two months before admission she suddenly discovered inability to recognize odors. She had not been able to recognize odors since. There was no history of uncinate fits.

Examination.—The neurologic findings were confined to the eyes, except for bilateral anosmia and questionable weakness in the left arm. The right eye presented secondary optic atrophy; the left showed normal fields for both form and color. The visual acuity of the left eye was 6/9. There was limitation of all extra-ocular movements of the right eye.

A roentgenogram showed a calcified mass in the region of both the greater and the lesser wings of the sphenoid bone (fig. 10). The pituitary fossa was of "top normal" size (11 by 12.5 mm.).

Operation.—On July 6, 1927, Dr. Frazier performed a right frontotemporal craniotomy. The tumor was readily exposed. It lay in the middle fossa, close to the sella turcica, arising from the greater and lesser wings of the sphenoid bone. It was only partially removed because of its great size and depth.

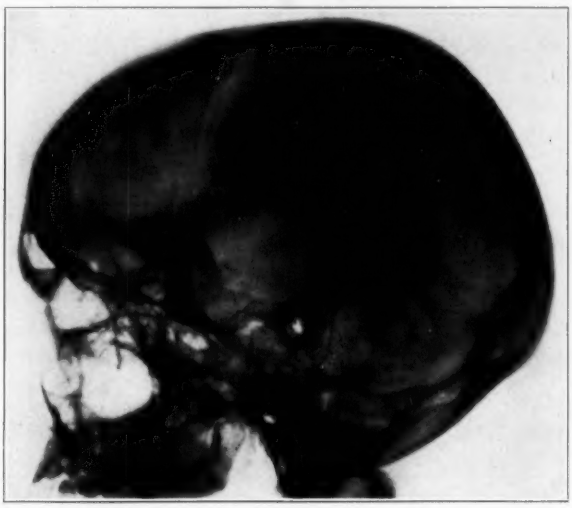

Fig. 10 (case 6).—Roentgenogram showing calcification along the sphenoid ridge.

Comment.—The neurologic findings were obscure. There was evidence of an increase in pressure within the skull, both in the ocular signs and in the increased manometric pressure. Inequality of the papilledema, which seems to be so characteristic of these cases, was present also in this case, since in one eye there was secondary optic atrophy and in the other 1 diopter of choking. The sensory jacksonian attacks were eventually explained by pressure of the postcentral gyrus against the skull.

The diagnosis was established by roentgen study, which showed a calcified tumor arising from both wings of the sphenoid bone.

In the next case the tumor covered the entire sphenoid ridge, extended into both the anterior and the posterior fossae and produced an interesting erosion of the roof of the optic foramen on the side of the tumor.

CASE 7.—*Large tumor of hour-glass shape straddling the entire right sphenoid ridge. Visual disturbances for four months. Five diopters of choking in the left eye; none in the right. Visual acuity: left eye, 6/9; right eye, 6/12. Visual fields normal. Horizontal nystagmus to the left. Right hyposmia. Slight right lower facial weakness. Increased intracranial pressure to 300 mm. of water. Erosion and increased depth of the floor of the pituitary fossa on the left; the measurements were: 8 by 8 mm. on the right; 11 by 11 mm. on the left. Operation and complete removal of a fibroblastoma.*

History.—E. G., a woman, aged 40, who was referred to Dr. F. C. Grant by Dr. A. L. Heck, of Wilmington, Del., gave a history that was rather brief, the difficulty concerning the eyes chiefly. Four months before entrance to the hospital she had an attack of double vision, which lasted for from ten to fifteen minutes. She did not know which eye was affected, but after repeated attacks found that by holding the left eye closed vision was clear in all directions. Following the first attack of diplopia there had been blurring of vision. At times, she experienced flashes of light or spots before the eyes. There were no symptoms suggestive of increase in intracranial pressure or signs of a localizing nature. She was admitted to the hospital because of obscure visual disorders.

Examination.—Neurologic examination gave confusing results. There was impairment of the sense of smell on the right. The left disk showed papilledema of 5 diopters; the right was normal. The visual acuity was 6/9 on the left, and 6/12 on the right. The visual fields were normal. There was horizontal nystagmus on lateral gaze to the left. No ocular palsies were elicited. There was slight right lower facial weakness. The tongue deviated slightly to the right; the uvula also turned slightly to the right. There was a positive Hoffmann sign in the right hand. The spinal fluid pressure was 320 mm. of water.

Roentgenograms disclosed erosion of the floor of the pituitary fossa, with an increase in depth on the left side. There was also some erosion of the dorsum sellae. The sella turcica measured 8 by 8 mm. on the left, and 11 by 11 mm. on the right. The optic foramen was eroded on the right side (fig. 11). The posterior clinoid processes were intact, and the anterior clinoid processes were normal. Roentgen study of the sinuses revealed clouding of the frontal sinuses bilaterally, clouding of the posterior ethmoid cells of the right side and a slightly increased density of the left maxillary sinus. The sphenoid sinuses were clear.

Ventriculography.—Sagittal views showed a definite displacement of the ventricles to the left. The left lateral ventricle was normal in size and shape; the right was considerably deformed by pressure exerted from the right side, resulting in an absence of the anterior horn on the right side.

Operation.—On Feb. 15, 1933, Dr. F. C. Grant performed a right transfrontal craniotomy. After uncapping the right frontal lobe a large encapsulated tumor presented. It was situated anterior to the lesser wing of the sphenoid bone, overlying the medial portion of the orbital roof (fig. 12). On removal, a second portion of the tumor, almost equally large, was seen lying behind the greater wing of the sphenoid bone in the middle fossa. It was adjacent to the pituitary fossa. This was removed without difficulty. Thus, the tumor sprang from the dura overlying the great wing of the sphenoid bone and extended into the anterior and middle fossa.

Pathologic Changes.—The tumor weighed 144 Gm., and measured 5 by 6 by 4 cm. It was a typical meningeal fibroblastoma, which was well differentiated and contained collagen and fibroglia in varying abundance.

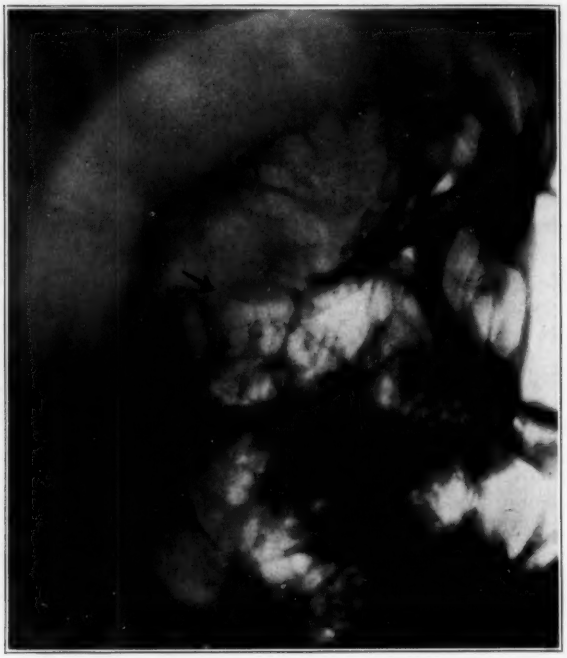

Fig. 11 (case 7).—Erosion of the roof of the orbital canal (indicated by the arrow) on the side of the tumor.

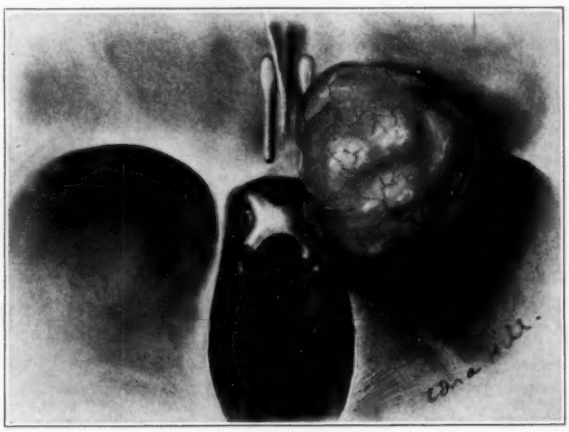

Fig. 12 (case 7).—A large tumor covering practically the entire sphenoid ridge, with signs of involvement of the anterior and the middle fossa.

Comment.—Diagnosis in this case was obscure. The history was not helpful, but there were concrete signs of increased pressure. However, none were particularly valuable in the determination of the location of the tumor. The history was brief, being of only four months' duration. Decreased sensation of smell was found on the right side. Papilledema was present, but was confined to the right eye, while the left gave no evidence of choking. On the other hand, visual acuity was better on the right, despite the papilledema. There were no demonstrable changes in the visual fields as to either form or color. The spinal fluid pressure was much increased. There were obscure signs in the cranial nerves, indicating possibly, but not definitely, central involvement of the right seventh and twelfth cranial nerves.

Little if anything of localizing value was obtained from the neurologic examination. X-ray pictures of the region of the sella turcica, however, were helpful, showing erosion of the left side of the sella turcica and increase in depth on this side. The right optic foramen was deformed, with complete absence of the upper half. Because of a definite question of the laterality of the tumor ventriculography was performed and showed absence of the anterior horn of the right lateral ventricle. Operation revealed a tumor arising from the right sphenoid ridge, extending into the anterior and middle fossae.

This case represents a rather advanced example of tumor of the sphenoid ridge with, however, very few clinical signs. The unilateral papilledema on the side of the tumor still remains unexplained. Diagnosis was established by roentgenograms and a ventriculogram. The absence of hemianopia is explained by the fact that the tumor did not extend far enough medially to compress the optic chiasm or tract. It represents a type of tumor arising from the greater wing of the sphenoid bone on the lateral aspect of the sphenoid ridge.

Sometimes tumors of the sphenoid are associated with unilateral exophthalmos, a feature which is well illustrated in case 8.

CASE 8.—*Tumor of the left sphenoid ridge arising from the greater wing. Progressive symptoms for four years. Exophthalmos of the left eye. Blindness of the left eye. Vision in right eye, 6/5. Right field normal. Bilateral choking of 2 diopters, with postpapillitic atrophy. Loss of sense of smell. Spinal fluid pressure, 38 mm. of mercury. Enlargement of the sella turcica to 13 by 12.5 mm. Operation.*

History.—E. M. G., a man, aged 31, who was referred to Dr. C. H. Frazier by Dr. P. W. Miller, of Hagerstown, Md., with a diagnosis of tumor of the brain, for four years had been suffering from severe frontal headaches which were more marked over the left eye. The eyes had been repeatedly refracted for glasses, but these had given only temporary relief. Three and a half years before admission he had had the first convulsion. The attack had lasted five minutes, and was attended by generalized clonic movements and loss of consciousness. The attacks were followed by severe pain in the left eye. They recurred every three months

from the time of their onset. There was a positive Wassermann reaction, and he was treated without effect. One year before admission to the hospital, unilateral exophthalmos appeared on the left side. Six months later the left eye had lost vision. Six weeks before entrance, vision in the right eye began to fail.

Examination.—There was bilateral anosmia. The left eye showed definite exophthalmos. The pupils reacted sluggishly to light, the left being larger than the right. The left eye was blind; the right had 6/5 vision, with a normal visual field. The disks showed postpapillitic atrophy and swelling of 2 diopters. There were coarse tremors of the entire right arm, which were not constantly present. The tongue and muscles about the mouth showed fibrillary tremors. The left achilles and patellar reflexes were slightly increased. There was an abortive ankle clonus on the right. The spinal fluid pressure was 38 mm. of mercury. The Wassermann reaction was strongly positive.

Roentgen examination of the head showed that the pituitary fossa measured 13 by 12.5 mm. There was decided clouding of the left maxillary sinus, with slight clouding of the left ethmoid sinus.

Operation.—A two-stage frontal craniotomy was performed by Dr. C. H. Frazier. At the second operation the tumor was seen arising from the left sphenoid ridge, both greater and lesser wings. It extended equally into the anterior and middle fossae.

ANALYSIS OF SIGNS

Eyes.—The ocular signs are important in tumors of the sphenoid ridge. Usually, in tumors of the lesser wing there is primary optic atrophy, but there may be atrophy of one nerve head and papilledema of the other. In two of the cases of tumor of the lesser wing there was bilateral primary optic atrophy; in one there was optic atrophy of one side, with papilledema of the other (the Kennedy syndrome), and in another there were no changes whatever. In the greater wing group, on the other hand, papilledema is more characteristic. In none of the cases in the latter group was there primary optic atrophy. There was, however, an unequal papilledema. Thus, in one case there was no papilledema in one eye and 5 diopters in the other. In another there was secondary optic atrophy on one side and 2 diopters of choking on the other. In the other two cases there was bilateral papilledema.

Hemianopic field defects are the rule in cases of tumor of the lesser wing, compressing as they do the optic tract of one side. This is usually complete, but may be quadrantic. On the other hand, no hemianopic field cuts were observed in the cases of tumor of the greater wing.

Oculomotor paralysis may be found in some cases, particularly when the tumor has a paramedian position and compresses the oculomotor nerve. This was observed in two cases of the lesser wing group.

Exophthalmos is encountered occasionally—once in eight tumors. It is unilateral.

Roentgenographic Findings.—These played a rather prominent part in this group of tumors. While there was no finding which could be called pathognomonic for the entire group, there were some rather

TABLE 1.—*Summary of Cases*

			Visual Signs					Roentgen Findings in Region of Sella Turcica						Spinal Fluid Pressure, Mm. H_2O
Case	Age	Sex	Visual Acuity	Optic Atrophy	Papilledema	Fields	Exophthalmos	Measurement of Sella Turcica	Dorsum	Anterior Clinoid Processes	Posterior Clinoid Processes	Floor	Other Findings	
1	36	M	Right eye, 6/9 Left eye, 6/4	.....	.....	Left homonymous hemianopia (incomplete)	.....	12 by 11 mm	Rarefied	Negative	Negative	Negative	Calcified along clavus	140
2	37	M	Both eyes, 20/200	Bilateral primary	.....	Left homonymous hemianopia	.....	12 by 6 mm.	Slight atrophy	Some pointing	Negative	Negative	.....	160
3	32	F	Right eye blind	Right eye, primary	Left eye	Left inferior quadrantic cut	.....	.....	Complete erosion	Negative	Complete erosion	Thin and depressed	.....	320
4	66	F	Right eye, 1/40 Left eye, 2/40	Bilateral primary	.....	Right homonymous hemianopia	.....	12 by 11 mm.	Negative	Negative	Negative	Thin curved shadow about pituitary	.....	
5	55	M	Both eyes, 6/45	.....	Both eyes, 0.2 diopters	.....	.....	9 by 9 mm.	Negative	Negative	Negative	Negative	Pineal calcification; no shift	375
6	28	F	Right eye blind Left eye, 6/9	Left eye, secondary	Right eye, 1 diopter	Right eye blind; left eye, form and color	.....	11 by 11.5 mm.	Negative	Negative	Negative	Negative	Calcified mass over right sphenoid bone	300
7	40	F	Right eye, 6/12 Left eye, 6/9	.....	Left eye, 5 diopters	Negative	.....	On left, 8 by 8 mm.; on right, 11 by 11 mm.	Negative	Negative	Negative	Increased depth	.....	300
8	31	M	Right eye, 6/5 Left eye, blind; postpapillitic	Bilateral post papillitic	Both eyes, 2 diopters	Right eye normal; left eye, blind	Left eye	13 by 12.5 mm.	Negative	Negative	Negative	Negative	.....	528

suggestive roentgen changes. Kornblum [2] has recently established some characteristics of the parasellar group of tumors, particularly as represented by tumors of the middle fossa. He stated that the suggestive findings include primarily changes in the dorsum, which has a faint or indistinct outline. The posterior clinoid processes are usually intact, and he remarked that the size of the sella turcica is at the upper limit of normal, with a slight increase in the anteroposterior diameter. Unilateral erosion of the dorsum or the floor of the pituitary fossa sometimes occurs.

The presence of a large sella turcica in five of eight cases is suggestive, and is in agreement with the observations of Kornblum. This finding in itself is not of diagnostic value, but it may be suggestive in an otherwise doubtful case. In three instances there was erosion of the

TABLE 2.—*Ocular Findings*

Case	Optic Atrophy	Hemianopia	Papilledema	Exophthalmos	Hyposmia
Lesser Wing Group					
1	0	+	0	0	0
2	+	+	0	0	0
3	+ (right)	+	+ (left)	..	+ (right)
4	+	+	0	0	+
Greater Wing Group					
5	0	0	+	0	0
6	0	0	+	0	0
7	0	0	+	0	+
8	0	0	+	+	+

dorsum sellae, once to a marked degree. In two instances there was marked erosion of the posterior clinoid processes.

A sign which may be of great significance is unilateral erosion of the sella turcica, whereby one side of the pituitary fossa, including the dorsum, clinoid processes and floor, may be eroded by the adjacent tumor. This was present in one instance in our cases.

Attention may be directed to unilateral erosion of the roof of the optic foramen as a sign of diagnostic importance in these cases. This has been emphasized by Pendergrass, who was impressed by its significance not only in this group of tumors but in others as well. It was found in only one of our eight cases, but in most of them the technic used to demonstrate this finding was not known when the cases were studied, so that we cannot be sure that it might not have been demonstrated.

Motor Signs.—In four cases there were signs of motor weakness. In one case the weakness was limited to the cranial nerves and was of a

2. Kornblum, Karl: Deformation of the Sella Turcica in Tumors of the Middle Fossa, Am. J. Roentgenol. **31**:23 (Jan.) 1934.

central type, involving the seventh, tenth and twelfth cranial nerves of one side; in another instance there was a faciobrachial monoplegia; in a third, merely a central facial weakness, and in another hemiparesis involving the face, arm and leg. The occurrence of these findings has been explained by compression of the middle cerebral vessel or its branches, with consequent anoxemia and death of nerve cells. The position of the tumor is not such as to cause compression of the corticospinal pathways directly.

Olfactory Nerves.—In four cases there was unilateral disturbance in the sense of small, owing to extension of the tumor anteriorly and compression of the olfactory nerve.

Other Signs.—In one instance there was impairment of memory due apparently to interference with the functions of the frontal lobes by compression of the anterior cerebral vessels. While uncinate fits were not observed in our cases, they may occur owing to the proximity of the tumors to the area of the uncus. Impairment of taste was noted once, but the reason for it is not clear.

COMMENT AND SUMMARY

The group of cases reported includes only eight tumors, chiefly because primary tumors of this area are not numerous. If intrasellar and suprasellar tumors with extension into the parasellar area were included, the number of cases could be swelled considerably. This would defeat the purposes of the study, however, as the object is to clarify an obscure group of cases instead of to point out variations in the manifestations of an already well known group.

There is a natural division of the cases into two groups: (1) those arising from the lesser sphenoid wing, and (2) those arising from the greater sphenoid wing.

The Lesser Sphenoid Wing Group.—Four cases (cases 1, 2, 3 and 4) were of tumors [3] confined to the region of the lesser wing of the sphenoid bone; for this reason they were in intimate contact with the sella turcica and the vascular and nerve structures around it. In case 1 there were subjective complaints of visual disturbances; in addition, examination revealed complete paralysis of the right third nerve, with ptosis, loss of ocular movements and loss of pupillary reactions; left homonymous hemianopia; increased spinal fluid pressure; normal fundi; relatively normal visual acuity, and a normal sella turcica. In this instance the position of the tumor, compressing the optic tract and the right oculomotor nerve, explained fully the clinical findings. In case 2, the condi-

3. This erosion of the optic canals has been described by Dr. H. K. Pancoast in an article entitled "The Roentgen Diagnostic Significance of Erosion of the "Optic Canals in the Study of Intracranial Lesions," which is to appear in the Frazier memorial number of the *Annals of Surgery*, January, 1935.

tions were not so clear. There was a history of loss of vision, primary optic atrophy, right homonymous hemianopia, weakness of the right corner of the mouth and right hand, impairment of taste and hypopituitary disturbances in the presence of normal spinal fluid pressure and a relatively satisfactory sella turcica, in which there were some atrophy of the dorsum sellae and slight pointing of the anterior clinoid processes. The primary optic atrophy and the homonymous hemianopia indicated a lesion near the optic nerve and pathways, and the primary optic atrophy served to differentiate the lesion from others which could produce homonymous hemianopia. The central weakness of the face and hand and the impairment of memory were confusing, and tended to attract attention away from the base of the brain to possibly the precentral area or to the corticospinal pathway. These findings are explainable by compression of the anterior and middle cerebral vessels by the tumor, the former being in intimate association with the growth. Circulatory impairment or loss in the frontal and precentral areas accounts readily for these symptoms. The pituitary symptoms are difficult to account for, except possibly on the basis of compression.

In case 3, the tumor was medially placed, arising from the lesser sphenoid wing but extending into both the anterior and the middle fossae. It was much larger than either of the preceding tumors. The patient suffered from loss of vision for several years, and on examination was found to have optic atrophy in the right eye and papilledema in the left, with no vision in the former and 6/30 in the latter, with an inferior quadrantic cut in the left temporal field; slight impairment of the sense of smell on the right side; greatly increased spinal fluid pressure, and marked erosion of the posterior clinoid processes and dorsum sellae, with encroachment of the sellar floor on the sphenoid sinus. The tumor was so situated as to produce a Kennedy syndrome involving the right optic nerve and tract and the right olfactory nerve, and to press against the pituitary fossa.

In case 4, there is a typical picture of a tumor of the lesser sphenoid wing, characterized by progressive loss of vision, bilateral primary optic atrophy, right homonymous hemianopia, impairment of the sense of smell on the right side and a sella turcica of "top normal" size.

The type of clinical syndrome to be expected, therefore, from tumors of the lesser sphenoid wing consists of a visual field cut, which is usually a complete homonymous hemianopia but which may be quadrantic, with localizing signs indicating involvement of the base of the brain, such as primary optic atrophy, a Kennedy syndrome, paralysis of the third nerve and unilateral impairment of the olfactory nerve. Other symptoms, such as motor paralysis of a central type (monoplegia), impairment of memory and pituitary disturbances, may be

present. The spinal fluid pressure is usually increased, but may be normal, and the sella turcica may be normal or may show changes similar to those described in parasellar lesions, indicated by a "top normal" size of the sella turcica, slight erosion of the dorsum and the anterior clinoid processes and unilateral deformation of the sella turcica in some instances.

The Greater Sphenoid Wing Group.—While the tumors comprising this group may be confined entirely to the greater wing of the sphenoid, they spread out to involve both the greater and the lesser wings. Of the four tumors in this group, one (case 5) was confined to the greater wing alone, while the other three (cases 6, 7 and 8) involved both wings.

In case 5, which was confined to the lateral portion of the greater sphenoid wing, the clinical syndrome was obscure and ventriculography was necessary in order to determine the location of the tumor. Besides, papilledema, increased spinal fluid pressure and the ataxia of the left arm and leg were not enough to establish the location. In this case, therefore, there was no clearcut syndrome.

The diagnosis in case 6 was established by roentgenograms, which showed calcification involving both the lesser and the greater sphenoid wings. Clinical examination showed secondary optic atrophy in one eye, a low degree of choking in the other and paralysis of the third nerve on the side of the tumor. The latter was evidence of involvement of the region near the lesser wing, but there was implication of territory more extensive than this region.

Localization was also difficult in case 7, which was one of a large tumor straddling the sphenoid ridge and extending into both the anterior and the middle fossae. The signs of increased pressure were marked, but the localizing neurologic signs were confined to hyposmia on the right side and a central palsy of the face, palate and tongue. Roentgen studies in this case revealed erosion of the roof of the right optic foramen and increase in depth of the sella turcica on the left side. The latter was due to a midline shift to the left with pulsating pressure against the sella turcica by the expanding third ventricle. Ventriculography alone established the diagnosis with certainty, though the erosion of the optic foramen would have been sufficient if its significance had been understood at first.

In some instances the tumors which arise from the sphenoid ridge may be accompanied by unilateral exophthalmos. This is illustrated by case 8, in which there were, in addition, papilledema, anosmia and a very slight enlargement of the sella turcica.

The clinical syndrome of these tumors arising from the greater sphenoid wing is not as decisive as that in the lesser wing group; yet

there are certain distinctive features which form a contrast to the latter. There is usually papilledema, which is sometimes unilateral, being associated often with secondary optic atrophy, usually on the same side as the tumor, sometimes unilateral exophthalmos on the side of the tumor, no changes in the visual fields, often impairment of the sense of smell on the same side as the tumor if the latter has extended into the anterior fossa, frequently associated with motor weakness of cortical nature and sometimes associated with roentgen findings of destruction, such as erosion of the roof of the optic foramen, and often a sella turcica of "top normal" size.

In the lesser wing group there are usually optic atrophy and homonymous hemianopia, while in the greater wing group there is papilledema, associated often with secondary optic atrophy located on the side of the tumor. Hemianopic field defects are absent as a rule. There is a greater likelihood of involvement of the structures near the sella turcica by the tumors of the lesser wing, hence occasionally paralysis of the third nerve results. In both types of tumor there may be involvement of the olfactory nerve due to extension into the anterior fossa, and in both likewise there may be partial paralysis of a monoplegic nature, due presumably to interference with the circulation in the cerebral vessels. The roentgen findings in both groups are helpful but not pathognomonic.

Differential Diagnosis.—The diagnosis of tumors of the lesser wing is not difficult. The presence of primary optic atrophy with hemianopic field defects and involvement of adjacent structures, such as the oculomotor or olfactory nerves, serves well to localize these tumors. They may, however, be confused with suprasellar or intrasellar tumors which have expanded into the parasellar region. Differential diagnosis is important in determining the surgical approach, since in the suprasellar group the approach would be frontal while in the lesser wing group it would be more easy by a lateral exposure.

The cases in the greater wing group offer more serious difficulties. They are often without distinctive neurologic findings. Except for papilledema there are few signs of value, with the exception of unilateral exophthalmos or unilateral anosmia. Careful roentgenographic studies are sometimes helpful in demonstrating unilateral erosion of the dorsum sellae or of the floor of the pituitary fossa. The diagnosis is possible, however, when one has a case with few signs, but with papilledema, unilateral anosmia and roentgenographic evidence of a sella turcica of "top normal" size, with some increase in the anteroposterior diameter and erosion of the dorsum. The clinical picture is somewhat confused at times by the pressure motor paralysis, often of a monoplegic nature. This is due in our estimation not to compression

of the corticospinal pathways or to involvement of the precentral area but rather to vascular compression with resulting anoxemia.

In four of the reported instances there was abundant roentgen evidence of sinus disease, and in one instance operation was deferred because of a diagnosis of sinus disease. It is necessary to be cautious in attributing intracranial disorders to sinus disease, particularly in the presence of papilledema or even of primary optic atrophy with field cuts. Sinus disease may exist with a tumor of the brain, and it is too easy to attribute obscure cases in which localization is difficult to sinus disease. The practice becomes particularly dangerous because of the well known fact that disease of the optic nerve may result from infection of the sinuses. It is a good working rule in such cases not to make a diagnosis of sinus disease when there is a suggestion of tumor of the brain and when the findings do not lend themselves to definite localization. It is better to look on them as tumors of the brain and to observe them carefully for the development of further localizing signs. In the presence of true papilledema it is wiser not to attribute the findings to sinus infection.

Pathologic Changes.—Tumors arising directly from the sphenoid ridge are encapsulated. They are roughly round or oval, with a smooth or lobulated appearance. Sometimes they are said to be flat. They vary from 4 to 5 Gm. in weight and from 1 to 2 cm. in diameter to 150 Gm. in weight and 5 or 6 cm. in diameter. They are adherent to the dura overlying and adjacent to the sphenoid ridge. Like tumors of this nature elsewhere in the brain, they often invade the dura, and because of the difficulty of removing this membrane at the base of the skull insurance against recurrence of the tumor is not absolute. Sometimes the tumors become calcified, as in one of our cases. They may cause hyperostosis of the bones at the base of the skull, which may be very extensive, but we were unable to demonstrate it in any of our cases. Sometimes the tumors invade the orbit, producing a nonpulsating exophthalmos. This was present in only one of our cases, but has been reported frequently by some in tumors in this location.

Tumors in relation to the sphenoid ridge may occupy the lesser sphenoid wing, the greater wing or both. They may be entirely confined to the medial aspect of the lesser wing. Usually the tumors of the lesser wing are small and are rather closely confined to the vicinity of this wing, while those in relation to the greater wing tend to extend into the anterior or the middle fossa or both. Occasionally the tumors arise from the anterior edge of the ridge and extend anteriorly, or from its posterior edge and extend into the middle fossa. Usually the tumors compress one or both optic nerves and the optic tract on one side when they are in contact with the lesser wing; they may likewise compress

the olfactory nerve of one side, the oculomotor nerve, the uncus and, the internal carotid, the middle cerebral or the anterior cerebral vessels. The tumors of the greater wing compress the lower part of the temporal lobe and the olfactory nerve of one side, and may extend far enough back into the middle fossa to compress the gasserian ganglion.

The histology of the tumors is of interest. Some are typical meningeal fibroblastomas. In six of our eight cases histologic specimens were prepared; in three the structure was typical of a fibroblastoma; in three others the histologic nature did not conform to the usual fibroblastoma structure. In all of these the tumors were encapsulated and small; the cells were arranged in small groups, like alveoli, around which was a thin strand of supporting tissue which was spread throughout the entire tumor. The cells were large, the nuclei vesicular and the cytoplasm extensive. The great vascularity and the alveolar arrangement of the cells have not been seen in fibroblastomas elsewhere in the cranium. The classification of this group of tumors offered great difficulties, but we concluded that they were probably a type of meningeal fibroblastoma. Despite their unusual vascularity and their atypical architecture, the important fact remained that the type cell was probably a fibroblast, and for this reason the tumors were classified as meningeal fibroblastomas.

CONCLUSIONS

1. An analysis of four encapsulated tumors of the lesser wing of the sphenoid bone and a like number of the greater wing is presented.

2. The lesser wing group is characterized by a definite syndrome.

3. In the greater wing group no clearcut syndrome could be designated.

FAMILIAL ORGANIC PSYCHOSIS (ALZHEIMER'S TYPE)

K. LOWENBERG, M.D.
AND
R. W. WAGGONER, M.D.
ANN ARBOR, MICH.

Alzheimer's disease (presenile dementia) was originally regarded as a clinical and pathologic entity. Recent reports of the occurrence of the disease as early as the second and third decades of life, however, preclude the conception of this syndrome as a presenile phenomenon. The following report is presented because of its unusual clinical and pathologic interest. It is unique in that it concerns the appearance of the disease in several members of a family and in two generations. We made both clinical and pathologic studies of one member of this group.

REPORT OF CASE

History and Course.—Louis R., Jr. (no. 13 in the genealogical chart, fig. 5), the patient whom we examined and whose brain we studied, was born in 1895 and was always in good health except for some disturbance in the ears during the three years previous to admission to the Traverse City State Hospital. He left school when he was in the fourth or fifth grade to start work. He was a printer, worked steadily and was successful. He was good-natured, sociable, industrious and thoughtful of others but was inclined to be nervous and excitable for a few years before admission to the hospital. He was first seen in 1927, at the age of 32, when he was interviewed regarding his sister's condition. He gave an impression of being peculiar and somewhat unbalanced mentally. He was reticent in manner but talked about being nervous and said that he was "shaky" when nervous and that he liked to be as active as possible. During the next year he became excitable, his memory became poor and he finally lost his position because of forgetfulness. He brooded over this and would cry when he failed in some task.

In 1929, he was examined at the University of Michigan Hospital. He complained of feeling nervous and of being easily excited. The pupils reacted to light, and there was slight nystagmus on lateral deviation to the left. Vision was normal. The tendon reflexes were normal, and there were no pathologic reflexes. There was marked oral sepsis, and because of this several teeth were extracted. Otologic study revealed scars in the left ear drum and polypi in the left middle ear, chronic otitis media on the right side and septic tonsils. The Kahn reaction of the blood was negative.

During the following two years the patient continued to deteriorate gradually. His appetite was good, and he slept well but was drowsy during the day. He

From the State Psychopothic Hospital, Department of Neurology, University of Michigan.

apparently had no hallucinations during this time. His requests were usually childish. He frequently wandered from home, and although he was unable to remember dates and places he did not misidentify members of the family. He displayed little or no insight into his mental condition and thought that his "nerves were shattered." He would sometimes laugh and cry without provocation, and during a crying spell two weeks before admission to the Traverse City State Hospital on Oct. 4, 1930, he complained of sharp pains in the head.

Examination on admission showed a short, stout, well built man. There was considerable acne over the back and shoulders. He was edentulous. The chest and the abdomen were normal; the blood pressure was 108 systolic and 62 diastolic, and there was no evidence of arteriosclerosis. The pupils were sluggish. There was some tremor of the fingers on extension, but otherwise the reflexes were normal. He cooperated poorly. Mentally, he appeared confused, with clouded consciousness, but seemed to be fairly agreeable. There was a marked loss of memory for both remote and recent events. He could not do simple sums or recall his wife's name. He appeared apprehensive of his difficulty and made excuses for his failures. There was no evidence of delusions or hallucinations. He was practically unable to write. In October, 1931, he had a convulsion lasting several minutes, during which he cried out, rolled his eyes, made convulsive movements of the arms and frothed at the mouth.

We examined the patient on Nov. 6, 1931. He was apathetic but aware of his surroundings and fairly cooperative. There were irregular variable myoclonic movements of the muscles, particularly of those of the face and of the fingers of the left hand. The pupils were equal and reacted normally to light and in accommodation. He could rotate the eyes completely to the right but not quite completely to the left. The ocular fundi were essentially normal, and apparently there was no involvement of cranial nerves. The tendon reflexes were active and equal. The abdominal reflexes were normal on the left side and diminished on the right. There were no signs of involvement of the pyramidal tract on the right, but the tone was increased in all the extremities, and there were suggestive Babinski, Oppenheim, Gordon and Chaddock signs on the left. It was impossible to test carefully for sensation, but there appeared to be some changes in sensation on the left. The patient walked slowly, holding both arms flexed at the elbow in front of him without swinging them, and there was a definite tendency to fall to the right. There appeared to be some incoordination in the use of the right arm. On Dec. 2, 1931, the patient had another convulsion, which lasted only a few minutes and apparently left no ill effects; following this, however, he failed rapidly and was not as active and restless as he had been. He died on Oct. 21, 1932, at the age of 37. Several days before death there was noted a generalized spasticity, with spasmodic contractions of the extremities.

Gross Postmortem Examination.—The brain weighed 1,150 Gm. The convolutions were somewhat atrophic over the entire convexity, and the leptomeninges were slightly thickened and cloudy. All the visible vessels were thin-walled. On frontal section the gray matter was of approximately normal width but strikingly brownish and very distinctly outlined; the white matter was somewhat atrophic but otherwise showed no gross changes. The basal ganglia showed the same appearance as the gray matter. The ventricles were moderately enlarged, but the ependyma was smooth. The pons, medulla and cerebellum showed no gross changes.

Examination of the somatic organs disclosed terminal hypostatic pneumonia as the only important pathologic condition.

Histologic Examination of the Brain.—Leptomeninges: There were only moderate changes in the leptomeninges; in certain areas they appeared somewhat thickened and contained a few cells of the lymphocytic type and accumulations of greenish pigment. The blood vessels were normal.

Cortex: Pathologic changes involved the entire gray matter of both hemispheres, the basal ganglia and the brain stem, so that a single description can be given, although there were slight deviations in certain formations.

The first layer was of normal width, but its subpial fibers were somewhat thickened. The cell content was increased and consisted of moderate numbers

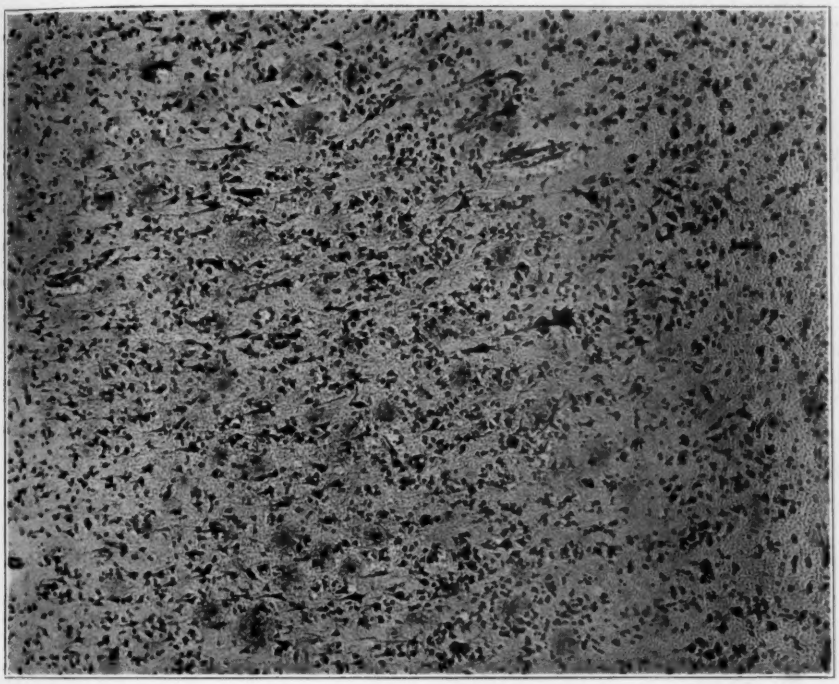

Fig. 1.—Photomicrograph of a section from the frontal region of the cortex, showing marked rarefaction of the cyto-architecture, involving all layers, nonspecific changes in the neurons and numerous senile plaques in all layers. Nissl stain; Zeiss planar, 20 mm.

of microglia and macroglia. The most striking feature was the presence of multiple typical senile plaques.

The cyto-architecture from the second to the sixth layer was markedly affected, all layers being rarefied and all sharing about equally in the loss, so that there were no localized foci (fig. 1). In a few areas in the frontal lobes, the upper layers (second and third) seemed to have suffered disproportionately.

The neurons themselves in sections stained by Nissl's method showed either far advanced simple atrophy, Nissl's "chronic cell disease," or various nonspecific types of disintegration and cell shadows. Alzheimer's changes could also be recognized in the intracellular fibrils.

In all layers there were countless typical senile plaques. These could be clearly demonstrated in sections stained with thionine, in which they appeared grayish blue (figs. 1 and 2). They were so numerous that the sections retained this color even after prolonged differentiation. Plaques with necrotic centers could be easily distinguished from those with a netlike structure. Both types frequently contained radiating microglial elements. The plaques did not show any relationship to the blood vessels (fig. 3).

There was very little glial activity, which was restricted to the formation of a few microglial and macroglial elements not related to plaques.

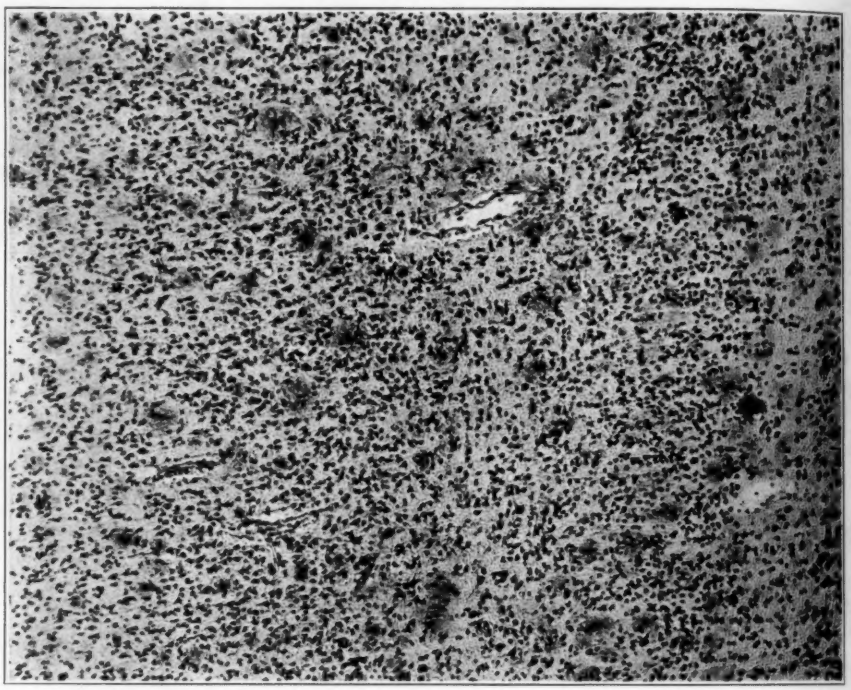

Fig. 2.—Photomicrograph of a section from the calcarine area of the cortex, showing numerous senile plaques in all layers. The cyto-architecture is fairly well preserved. Nissl stain; Zeiss planar, 20 mm.

The blood vessels seemed to be entirely undisturbed; there were no sclerotic changes. The process was fairly evenly distributed in the entire cortex, the occipital lobes being affected in the same way as the frontal and temporal lobes.

The cornu ammonis, frequently more involved than other areas in Alzheimer's disease, showed a far advanced stage of the disease, as did also the nucleus amygdalae.

Bielschowsky and Levaditi preparations revealed almost complete destruction of the tissue network; the senile plaques were so numerous that they frequently fused together, occupying almost the entire width of the cortex (fig. 3). In such areas there were left only isolated, fragmented, thickened, tortuous axis-cylinders. The glial structure seemed to be entirely necrotic. Alzheimer's fibrillar changes

were numerous and represented by all types of basket cells. In the cornu ammonis and a few other areas the plaques contained numerous well preserved microglial elements, giving them a stellate appearance.

Sections stained with scarlet red showed a small amount of fat in the few neurons still preserved, as well as occasionally in the perivascular spaces. Perdrau preparations showed an absence of connective tissue proliferation.

All layers of the white matter of both hemispheres contained senile plaques in moderate numbers. The macroglia were very active, and gold preparations disclosed numerous large astrocytes.

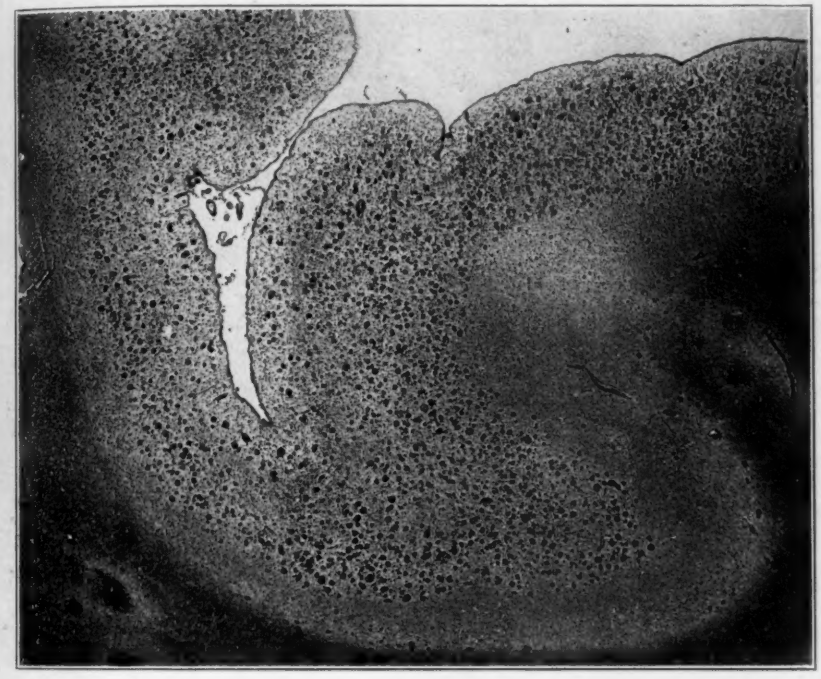

Fig. 3.—Photomicrograph of a section of the cortex, showing countless senile plaques in the gray matter. Levaditi stain; Zeiss planar, 50 mm.

Caudatum and Putamen: The parenchyma showed far advanced changes similar to those of the cortex. The large neurons were frequently reduced to shadows, and the smaller ones showed different types of degeneration. Both were characterized by countless plaques (fig. 4).

Pallidum: The parenchyma showed less severe changes, but some of the neurons were shrunken or reduced to shadows. There was moderate formation of plaques, and the number of microglia was somewhat increased.

Thalamus: The changes were less pronounced than in the putamen and pallidum, but a considerable number of neurons appeared to be shrunken, and there were a few scattered plaques. There was no glial response.

Bielschowsky preparations revealed no Alzheimer cell changes in the basal ganglia, and lipoids were present in negligible amounts.

Hypothalamus: There was advanced, nonspecific degeneration of the neurons as well as countless senile plaques. These were very numerous in the nuclei of the walls of the third ventricle, especially in the central gray substance, the nucleus paramedianus and the mamillary bodies. There were occasional senile plaques in the substantia nigra, the subthalamic bodies and the red nuclei. In these areas there was no glial or vascular response.

Fourth Ventricle: The nuclei in the floor of the fourth ventricle contained no senile plaques and showed only slight, nonspecific changes. The neurons of the olives were shrunken, but there were no plaques.

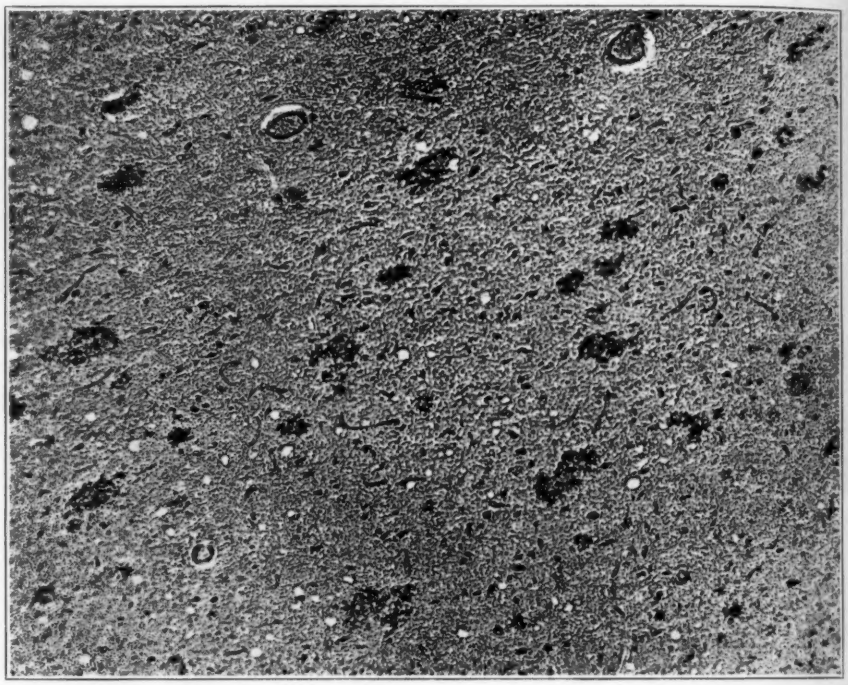

Fig. 4.—Photomicrograph of a section from the caudatum, showing numerous senile plaques. Levaditi stain; Zeiss planar, 20 mm.

Pons: There was slight, nonspecific degeneration in the pons, which was free from plaques.

The amount of fat in the hypothalamus, pons and medulla was negligible.

Ventricles: The ependyma was intact, but the choroid plexus contained accumulations of large lipoid cells resembling those seen in the syndromes described by Gaucher, Niemann and Pick, and Schüller and Christian. Many of these cells had undergone a fatty metamorphosis with deposits of cholesterol. Numerous pigment-laden macrophages were also present. In addition, there were calcification of the capillaries, formation of cysts and hyalinization of the supporting tissue.

Cerebellum: The Bergmann layer contained small numbers of microglia and macroglia. The Purkinje elements were markedly degenerated. The tigroid sub-

stance was absent in some cells, and the nuclei stained poorly. The granular layer appeared to be normal, but the white matter contained scattered senile plaques. The neurons of the dentate nucleus were either greatly shrunken or reduced to shadows.

Spinal Cord: The parenchyma showed Nissl's "chronic cell disease," with scattered senile plaques in the gray substance. The white matter, the glia and the blood vessels were apparently normal.

Summary of Postmortem Observations.—The brain was moderately atrophied, and the gray matter and basal ganglia were of a peculiar brown color.

Histologically, there were degenerative changes, such as reduction in neurons, dominated by the presence of countless senile plaques in all areas of the cortex, the basal ganglia, the hypothalamus, the spinal cord and the white substance of the hemispheres and cerebellum. Changes in the fibrils were frequently seen in the neurons of the cortex. The microglia remained uninvolved, but the macroglia showed considerable activity in the white matter. The connective tissue showed neither proliferative nor degenerative changes. Fat was present in negligible amounts in the brain and spinal cord. The choroid plexus showed some lipoid degeneration. The histologic picture of the brain corresponded to that of so-called Alzheimer's disease.

DATA ON OTHER MEMBERS OF THE FAMILY

Louis R., Sr. (no. 7, fig. 5), the father of Louis R., Jr., was of French descent. His parents both died at a relatively late age. His father was an alcoholic addict and married his first cousin, who had several paralytic strokes, with serious mental deterioration. Louis R., Sr., had two brothers. One had a "nervous breakdown," and the other died of a paralytic stroke. So far as is known he was healthy until the age of 31, when following a "stroke" there developed a mental condition associated with severe headaches. He became "apathetic" and believed his wife to be unfaithful. A month after the onset of this condition he was admitted to the Traverse City State Hospital in a very weakened condition, being unable to stand without assistance. He was incontinent of urine and feces, drooled saliva and was disoriented. No physical abnormality was found to account for his condition. Ten days after admission he became excited, his temperature was 102 F. and his pulse was irregular and weak. During the first six weeks of hospitalization the condition was variable, although he remained weak and appeared to "brood a great deal." About this time he had a "severe seizure" and was in bed for three days. A week later he had another seizure. The condition gradually became worse, and he died seven months after admission to the hospital, at the age of 32, on April 8, 1902.

His wife (no. 8), the mother of Louis R., Jr., died of cancer; her father was an alcoholic addict, who died at the age of 68; her mother died of a "stroke" at the age of 75. Her brother also used alcohol excessively.

A sister of Louis R., Jr., Ella R. S. (no. 11), was admitted to the Traverse City State Hospital at the age of 36. So far as is known she was normal and healthy until about one year before admission. She went to school until she reached the ninth grade and was a good student. She was sociable and even-tempered. She married at the age of 18. The condition which caused her commitment to the hospital began at the age of 35 with delusions of persecution and outbursts of uncontrollable temper. Physically, she was small and undernourished. The blood pressure was 140 systolic and 80 diastolic, and the pulse was

weak and irregular. She had difficulty in swallowing and had to be fed with a a spoon as she was unable to hold a dish or to bring food to her mouth. She had frequent generalized convulsive movements. There appeared to be a loss of voluntary control, and coordination was poor. In sitting she inclined to the left, apparently being unable to sit up straight. The reflexes were exaggerated, but there were no pathologic reflexes. Vision appeared to be poor. The pupils were small and reacted to light and in accommodation. There appeared to be no difficulty in hearing. The gait was unsteady, and she tended to fall to the left. There was tremor of both hands and of the tongue. Mentally, she appeared confused and apathetic, although at times she made an effort to be cheerful. There was a marked speech defect, and her enunciation was poor, so that no one could understand what she said. She indicated assent or dissent by shaking her head. She denied hearing voices; she appeared disoriented but seemed to understand simple questions and answered them correctly by shaking her head. The Was-

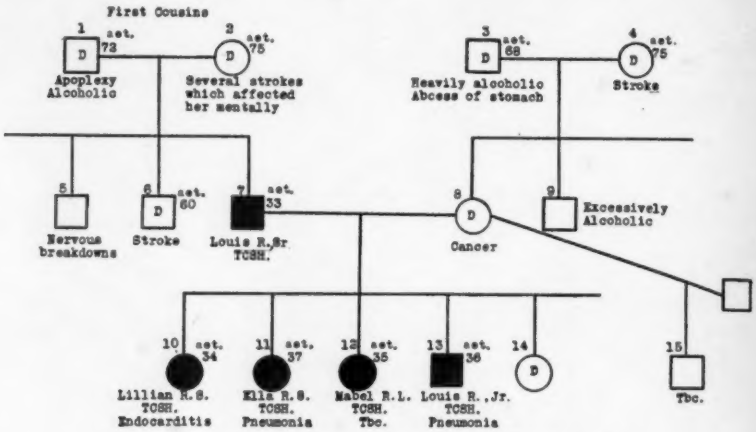

Fig. 5.—Genealogical chart of the afflicted family.

sermann reaction of the blood was negative; that of the spinal fluid was reported as one plus; the mastic and Lange tests were negative. She gradually failed from the time of admission and became very unsteady and was able to get about only by holding on to chairs and tables. Several months before death she became entirely helpless and had to be cared for as a child. There was hypertonicity of the muscles of mastication, which made it necessary to give her liquid food and to use a feeding cup. On one occasion she had an epileptiform convulsion, and late in the illness she appeared to be entirely out of touch with her surroundings. A few weeks before death there were several epileptiform convulsions. She died of bronchopneumonia at the age of 36, on Dec. 4, 1925.

Mabel R. L. (no. 12), married, a housewife, a sister of Louis R., Jr., was admitted to the Traverse City State Hospital at the age of 35. Little was known of her personal history. Two years before admission she began to make occasional irrelevant remarks and became more quiet. For a year before admission she was less particular about housework and lost interest in her personal appearance. She was forgetful and unable to remember what to do in cooking. She made no complaints but wept frequently. It was necessary to bathe her and look after her clothing. Two and a half months before admission she had a convul-

sion and was found by a neighbor. She was more confused for a few hours after this attack but later was as she had been before. At times she would talk to herself and laugh in a silly manner and was unable to answer questions coherently. Physical examination revealed a well developed, rather plump woman, whose chest was undeveloped and thin. She weighed 127 pounds (57.7 Kg.). The blood pressure was 132 systolic and 78 diastolic. The reflexes were normal. There was some cyanosis of the feet. Mentally she showed an attitude of indifference, was rather uncooperative and responded only after numerous questions. Her replies were fragmentary, incoherent and irrelevant. She would occasionally laugh in a silly manner and then lapse suddenly into indifference. There was a mild speech defect. After admission to the hospital she had to be dressed and fed; she paid no attention to her bowels or bladder. Three months after admission she had a convulsive attack which lasted for about fifteen minutes. After the attack she grew rapidly worse, drooled saliva and took only liquid nourishment. She failed rapidly and died thirteen months after admission, on Oct. 15, 1928. Autopsy revealed pulmonary tuberculosis, chronic cholecystitis and cholecystolithiasis. The brain was small and appeared shrunken, weighing 900 Gm. The convolutions were atrophic, especially over the frontal lobes, and there was moderate atrophy of the parietotemporal areas. Nothing further was noted on section.

Lillian R. S. (no. 10), a sister of Louis R., Jr., was admitted to the Traverse City State Hospital at the age of 32. She was married and had had six children. Her husband noticed that she worried a great deal about her work for several weeks before admission. Following the birth of her last child, five weeks before admission, her memory was affected. She was disoriented as to time and could not work. She would put wrong ingredients in food and forget to take things out of the oven. She exhibited no spontaneity. Her body was filthy. The pupils were irregular and reacted slowly to light. There was a fine tremor of the tongue on protrusion. The reflexes were all normal. She was unable to do the finger-to-nose test. Her speech was dysarthric, and in repeating the alphabet she would omit and transpose letters. Physically, she appeared well nourished but of small stature. She weighed 99½ pounds (45.07 Kg.); the blood pressure was 122 systolic and 98 diastolic. Mentally she was confused and disoriented. During her stay in the hospital she was frequently depressed and in a bad mood. She complained of blood rushing to her head and thought that she saw angels. During the year preceding death she deteriorated rapidly, and it became almost impossible to communicate with her. She died two and one-half years after admission, at the age of 35, on Oct. 4, 1922.

SUMMARY

The clinical course of the disease in all the affected members of the family was practically identical. The disease began early in the fourth decade of life: in Louis R., Sr., the father of our patient, Louis R., Jr., and in Lillian R. S., a sister, at the age of 31; in Louis R., Jr., at 32; in Mabel R. L., a sister, at 33; in Ella R. S., a sister, at 34. The duration of the disease varied somewhat: Ella R. S. was ill for approximately two years; Louis R., Sr., for two or three years; Lillian R. S., for approximately three years; Mabel R. L., for approximately four years and Louis R., Jr., for six or seven years.

The disease began gradually in the four siblings. Lillian R. S. at first appeared depressed and could not manage her daily work; she became worse following childbirth. In Louis R., Jr., the development of the disease was very slow, with "nervousness and excitability." He remained in this condition for approximately two years (1927 to 1929). In September, 1929, he was considered to be constitutionally psychopathic. During 1930, the mental deterioration became so evident that he was admitted to the Traverse City State Hospital with a far advanced psychosis. The second sister, Mabel R. L., appeared changed mentally approximately one year before admission to the hospital, with seclusiveness and apathy as the outstanding symptoms. The third sister, Ella R. S., also had mental symptoms one year before admission; her condition closely resembled that of Louis R., Jr. Nothing is known, however, of the prodromal stage in the case of Louis R., Sr., in whom the disease began abruptly with a "seizure" (epileptiform?).

Nervousness, irritability and progressive loss of memory were observed in all the patients. Even during the prodromal period the patients needed constant care and supervision. In two (Louis R., Sr., and Ella R. S.), there was also progressive physical deterioration necessitating care in bed early in the course of the disease. The other three siblings remained in fair health for a relatively longer period.

Epileptiform seizures, which occurred in all the patients except Lillian R. S., constituted an early and important evidence of the disease. These seizures lasted for from five to fifteen minutes. None of the patients died during a convulsion although the condition of Mabel R. L. became decidedly worse following a seizure. The number and frequency of the seizures varied: Louis R., Sr., suffered a seizure approximately one year before admission, and two, twelve days apart, toward the end of his illness; Louis R., Jr., had two seizures, six weeks apart, ten or eleven months before death, and Mabel R. L. had two seizures approximately one-half year apart, the second occurring about ten months before death. Ella R. S. had numerous seizures, which prostrated her toward the end of her illness. She suffered from peculiar muscular twitchings, which made walking and even sitting impossible. Similar symptoms occurred in Louis R., Sr.; it is stated that his muscles twitched constantly. Louis R., Jr., had muscular twitchings of an irregular, myoclonic type.

A speech defect, variously described as slurring, incoherence, dysarthria and even mumbling, was another important early manifestation. The most advanced disturbance of speech occurred in Ella R. S., in whose case the clinical course was stormy and speech became incoherent and mumbling at a time when she was still able to understand questions. Mabel R. L. also had a disturbance of speech, but the type

was not recorded. Louis R., Sr., had a pronounced disturbance, and the speech of Lillian R. S. and of Ella R. S. was described as dysarthric. In examining Louis R., Jr., approximately one year before death we found his speech very slow but without definite dysarthria.

In all five patients the clinical course was dominated by increasing mental disability and confusion and finally by a completely vegetative state. Communication with the patients was rendered impossible at the height of the illness.

The neurologic signs were less constant and of minor significance. Most of the reflexes were somewhat exaggerated; pathologic reflexes were not regularly present. Ella R. S. showed ankle clonus and positive Romberg and Babinski signs. About a year before death, Louis R., Jr., had positive Chaddock and Gordon signs on the left side. Advanced deterioration precluded testing for changes in the sensory field.

A sluggish reaction of the pupils was reported in the cases of Ella R. S. and Lillian R. S. The pupils of Mabel R. L. and Louis R., Jr., reacted normally.

The blood pressure was normal in the four patients for whom it was determined: Ella R. S., 140 systolic and 80 diastolic; Mabel R. L., 132 systolic and 72 diastolic; Lillian R. S., 122 systolic and 98 diastolic; Louis R., Jr., 108 systolic and 62 diastolic. Signs of peripheral arteriosclerosis were absent. Laboratory studies of the blood and the spinal fluid were made for Mabel R. L. and Louis R., Jr.; they gave normal results in every respect except that a one plus Wassermann reaction of the spinal fluid was reported once for Ella R. S.

The immediate cause of the death of Lillian R. S. was said to be endocarditis, but this was not verified by autopsy; Mabel R. L. died of pulmonary tuberculosis, chronic cholecystitis and cholecystolithiasis (verified at autopsy). Louis R., Jr., died of hypostatic pneumonia; the immediate cause of death for Ella R. S. and for Louis R., Sr., is not known.

Death occurred in all the patients about the middle of the fourth decade of life, and the four siblings died within a single decennium (1922 to 1932).

Because of the anatomic and histologic picture in the brain of Louis R., Jr., and the advanced atrophy of the brain of Mabel R. L. and the clinical picture as detailed, we may conclude that all five members of the family suffered from an organic psychosis of the Alzheimer type.

COMMENT

Study of the clinical picture of Alzheimer's disease described in the literature reveals a close conformity to the findings in our subject.

Schottky,[1] who examined female patients exclusively, could determine no constant body type. Of our three female patients, two were small and of medium build; the third (Mabel R. L.) was described as "strongly" built. Our two male patients were described as of "muscular" type. In accordance with Schottky,[1] we found no peculiar constitutional characteristics.

The disease is insidious, which makes it difficult to determine the duration of the prodromal phase. According to Schottky,[1] the first striking symptoms occur from several months to one year after the actual onset of the disease, and this may be true in many instances. Of our patients, Louis R., Jr., and Mabel R. L. had a prodromal phase of approximately two years; Ella R. S., of approximately six months, and Lillian R. S., of approximately two months. Nothing definite is known concerning the prodromal stage for Louis R., Sr., in whom the disease supposedly began suddenly.

The duration of the disease varies greatly, some cases of twenty years' standing having been observed (Barrett,[2] Bett,[3] Grunthal[4]) and others in which it lasted from twelve to thirteen years. In the vast majority of cases, however, the duration is much shorter, seldom exceeding from two to four years. Louis R., Jr., was ill five or six years; Mabel R. L., approximately three years; Lillian R. S., approximately two and three-quarters years; Louis R., Sr., approximately twenty months, and Ella R. S., sixteen months (the prodromal period being included in all cases). Rapid and progressive deterioration, an outstanding symptom according to all authors, was present in all of our patients.

A number of neurologic findings have been noted by all authors. Sluggish pupils, a symptom which may be intermittent (Runge[5]), are frequent. This phenomenon occurred in two of our patients (Lillian R. S. and Ella R. S.). Facial paralysis is common (Spielmeyer[6]). Louis R., Jr., had incomplete facial paralysis, but nothing is known concerning this symptom in the other patients. Schottky[1] called attention

1. Schottky, J.: Ueber präsenile Verblödungen, Ztschr. f. d. ges. Neurol. u. Psychiat. **140**:333, 1932.

2. Barrett, Albert M.: Degenerations of Intracellular Fibers, Am. J. Insanity **67**:503, 1911.

3. Bett, quoted by Barrett.[2]

4. Grunthal, E.: Ueber die Alzheimersche Krankheit, Ztschr. f. d. ges. Neurol. u. Psychiat. **101**:128, 1926.

5. Runge, O.: Die Geistesstörungen des Umbildungsalters und der Involutionszeit, in Bumke, O.: Handbuch der Geisteskrankheiten, Berlin, Julius Springer, 1930, vol. 8, p. 597.

6. Spielmeyer, W.: Die Psychosen des Rückbildungsalters, in Aschaffenburg G.: Handbuch der Psychiatrie, Vienna, Franz Deuticke, 1912, vol. 5, p. 85.

to a blank facial expression in some of his patients. We observed this in Louis R., Jr., and Ella R. S.

In Alzheimer's disease the reflexes are usually not of significance, being either slightly increased or decreased. Increased reflexes were seen in Lillian R. S., and pathologic ones, in Louis R., Jr., and Ella R. S.

A great deal of attention has been drawn to the disturbances in speech, which may appear early and vary in character. According to Schottky,[1] the speech may be slow in the beginning or abrupt and slurred, and marked articulatory disturbances may be associated with paraphasic mutilations. A speech defect may appear suddenly following a seizure. Disturbances of movement of the tongue, stereotyped chewing and smacking are not infrequent; these occurred in Ella R. S. and Louis R., Sr. The speech of Louis R., Jr., became slow but remained intelligible.

Restlessness and excitability, expressed by many patients in an aimless overactivity, may or may not occur in Alzheimer's disease, as some of the patients appear dull and quiet. Our patients represented both groups. Louis R., Sr., was overactive and restless and had to be restrained. Louis R., Jr., was restless and excitable during the first two years of the illness but dull afterward. Mable R. L. was dull most of the time.

Disturbances of sensibility in Alzheimer's disease are but little known, their determination being impossible in deteriorated patients. Schottky [1] was of the opinion that some of the patients have unpleasant sensations; he observed spasms of the stomach and intestines in one case, which he was able to verify roentgenologically; another patient suffered from hyperesthesia of the entire left side. Astereognosis and adiadokokinesis may also be present. It was impossible to test the sensibility of our patients except in the case of Louis R., Jr., in whom pain sensation seemed to be somewhat decreased although he was able to feel a pinpoint approximately a year before death. The sense of motion and of position was apparently retained on the right side but lost on the left. It was impossible to be sure of vibratory sensation.

Disturbances of gait and of posture are frequent. The gait is unsteady and staggering, so that the patients seem to crawl along the wall. They are clumsy about eating because of the tremor of the extremities (Schottky [1]). These symptoms were marked in several of our patients: Louis R., Sr., was unable to stand without support; Ella R. S. had a pronounced disturbance of gait and had to be supported or use objects to support herself, and she finally became unable to get about. She was likewise unable to feed herself.

Vegetative disturbances in Alzheimer's disease are of far greater importance than they have been considered to be. According to Schottky,[1] the rapid physical decline is a true marasmus in many instances. There was a very rapid decline in all our patients. Even if we exclude Mabel R. L., who died of pulmonary tuberculosis, and Lillian R. S., who probably died of endocarditis, we have to consider the physical failure in the remaining three cases as marantic. We noted, further, in our patients a number of symptoms which were clearly vegetative in origin: perspiration and drooling of saliva in Louis R., Sr., and cyanosis in Ella R. S. and Mabel R. L. There was also loss of control of the bladder and rectum in three patients: Louis R., Sr., Mabel R. L. and Ella R. S.

Seizures are well known in Alzheimer's disease. Schottky[1] distinguished different types of seizures: paralytic, apoplectiform and epileptiform. The apoplectiform seizures resemble coma; they may lead in some instances to an acute turn for the worse, in others to paralysis which disappears after a few hours. In Louis R., Sr., the illness began with what was considered an apoplectic stroke. The seizures of our other patients were apparently epileptiform. Seizures occurred in four of our five patients. Muscular twitchings, the relationship of which to convulsive attacks has not yet been positively established, are also frequently noted.

Spastic phenomena are not unusual. They may involve one group of muscles, for example the muscles of mastication (Ella R. S.), or one side of the body, as reported by Schottky,[1] or may result in generalized spasticity shortly before death (Louis R., Jr.).

The aimless overactivity of the patients has been analyzed by Herz and Fünfgeld,[7] who came to the conclusion that this symptom at first resembles normal activity. The patient carries out complicated and purposeful movements which attract attention because of their excessive amount; for example, Louis R., Jr., became overtalkative and easily excited, realizing that there was something wrong with himself. Later this hyperkinesis becomes less and less differentiated; complicated movements are no longer carried out. This stage was designated by Herz and Fünfgeld as primitive overactivity. Toward the end, even simple movements of the limbs are repeated over and over, and the stage of amorphous activity has been reached.

The disturbances of speech were analyzed by Fünfgeld and Herz[7] in the same way. The urge to speak is a function of the speech area which corresponds to the function of the motor mechanisms. Herz and Fünfgeld[7] spoke of "speech hyperkinesia," the urge to speak being con-

7. Herz and Fünfgeld: Zur Klinik und Pathologie der Alzheimerschen Krankheit, Arch. f. Psychiat. **84**:633, 1928.

sidered as a natural speech hyperkinesia. This was evident in Louis R., Jr., before signs of deterioration had definitely set in. With progressing deterioration primitive speech hyperkinesia occurs, only to be replaced later by amorphous speech hyperkinesia.

The overactivity and the disturbances of speech may be influenced by psychic components (Sterz [8]), but we agree with Schottky [1] that the organic changes in the brain are largely responsible. The disturbances in speech and the histologic changes responsible for them can be correlated if one presumes that the speech area suffers early and disproportionately in comparison with other areas.

The correlation of the disturbances in gait with the histologic changes is not yet clear, though Merzbach [9] expressed the belief that the caudate nucleus is responsible. However, Louis R., Jr., showed extensive changes of the caudate nucleus without having had any difficulty in walking; so Merzbach's [9] view cannot be regarded as proved.

The mechanism of the seizures has been given considerable attention in the literature. Krapf [10] analyzed a series of cases and concluded that the destruction of the brain tissue as such in Alzheimer's disease is not responsible for seizures. According to him, it is chiefly the high blood pressure, as well as the associated arteriosclerosis, which produces them. We cannot accept this explanation because in the four of our patients for whom the blood pressure was known it was within normal limits, and none of them suffered from arteriosclerosis. We assume, therefore, that the destruction of the brain may well produce convulsions.

Our knowledge of the causes of the muscle twitchings, so impressive in some of our cases, is unsatisfactory. This problem may be linked with the chemistry of the body tissues and fluids and requires careful and elaborate metabolic studies.

Age and Heredity.—In the foregoing discussion it has been shown that the five cases described may be considered as instances of so-called Alzheimer's disease. There are, however, two deviations: (1) the early age of onset and (2) the factor of heredity, not previously observed in this condition.

It is generally accepted that this disease of the brain occurs in the fifth, sixth or seventh decade of life, the so-called presenile period. It had been observed in only one instance in the third decade (Malamud

8. Sterz, G.: Zur Frage der Alzheimerschen Krankheit, Allg. Ztschr. f. Psychiat. **77**:336, 1921-1922.

9. Merzbach, quoted by Schottky, J.: Ztschr. f. d. ges. Neurol. u. Psychiat. **140**:333, 1932.

10. Krapf, E.: Ueber die epileptiformen Anfälle bei Alzheimerscher und die Anfälle bei Pickscher Krankheit, Arch. f. Psychiat. **93**:409, 1931.

and Lowenberg [11]), and in one instance, in the fourth (Barrett [2]). Our five patients all died between their thirty-fourth and thirty-seventh years. A study of the literature suggests, however, that the disease may not unusually begin in the fourth decade, as happened in one of Schottky's [1] patients. It is probable that further investigators will discover more cases of the early type.

The occurrence of the ailment in persons of different generations (father and daughter) is probable in one of the observations of Schottky.[1] The disease has been seen in twins by von Braunmühl [12] (not yet reported). The usual hereditary factors reported by some of the authors are restricted to certain minor or major stigmas in the families involved. This is the case in the family R. The father (no. 1, fig. 5) of Louis R., Sr., was an alcoholic addict; he died suddenly at the age of 72. He married a first cousin (no. 2), who had several strokes and deteriorated afterward; she died at the age of 75. By this union there were three sons. One (no. 5) had "nervous breakdowns," of which the nature is not known; another (no. 6) died of a stroke at the age of 60; in the third, Louis R., Sr., Alzheimer's disease appeared for the first time. He married a woman (no. 8) of poor mental stock, whose father (no. 3) was an alcoholic addict and whose mother (no. 4) died of a stroke at 75. From this union (nos. 7 and 8) there were five siblings. One (no. 14) suffered a violent death and nothing is known concerning her mental state; the four others (Lillian R. S., Ella R. S., Mabel R. L. and Louis R., Jr.) became ill with the same disease of the brain, which annihilated all of them within a single decade.

All the patients of the second generation were married and had children. Ella R. S. had two children; one died of an unknown cause in early childhood, and the second, a daughter, now 25 is married and healthy. Mabel R. L. had two children, now 11 and 16 years of age, both healthy. Louis R., Jr., had two children, now 12 and 15 years of age and in good health. Lillian R. S. had five children; their ages and the condition of their health are unknown.

Classification.—The question of classification has been raised several times in recent years, and it appears at present more complicated than ever. The problem must be regarded from two angles: (1) clinical and (2) pathologic. From the clinical point of view, it seems justifiable to distinguish two different types: (*a*) the presenile type, which occurs in most of the cases, and (*b*) the juvenile type, at present very

11. Malamud, W., and Lowenberg, K.: Alzheimer's Disease, Arch. Neurol. & Psychiat. **21**:805 (April) 1929.

12. von Braunmühl, A.: Kolloidchemische Betrachtungsweise seniler und praeseniler Gewebsveränderungen, Ztschr. f. d. ges. Neurol. u. Psychiat. **142**:1, 1932.

restricted. In our cases the condition is neither presenile nor juvenile and shows such a distinct hereditary factor as to justify an additional subdivision.

Pathology.—From the pathologic point of view, the Alzheimer syndrome must be regarded as a single unit, but it can probably be produced by different etiologic factors. This view is supported by pathologic and experimental investigations. Malamud and Lowenberg [11] observed a peculiar change in the choroid plexus, which may be to some extent responsible for the disease. This change has been seen only once, so we must assume that in the majority of cases the etiology is different. We offer no explanation for the lipoid changes in the choroid plexus of Louis R., Jr.

Von Braunmühl [12] attempted to explain the histologic changes on the basis of colloidal chemistry. According to this author, the intracellular fibrils are highly susceptible to osmotic influences in the surrounding medium and react readily by swelling. The fibrils appear thickened, elongated and whorled. Bozler [13] produced similar phenomena in neurons of Rhizostoma by placing the animals in hypertonic sea water. Later, shrinkage of the fibers and changes in staining properties may follow. In applying these facts to the histologic changes in Alzheimer's disease, von Braunmühl [12] concluded that the colloids of the brain are unstable. Their minute particles may be subject to constant agglomeration, which results in a decrease of their dispersity, so-called syneresis. These changes are only partly reversible, so that there is an ostensible aging of colloids, so-called hysteresis. The hysteresis, according to Rudzicka,[14] leads finally to physiologic death. Von Braunmühl [12] pointed out that the changes in the fibrils and the senile plaques seen in Alzheimer's disease may be one of the products of syneresis. This may also cause various changes in the brain but does not necessarily mean an aging in the chronological sense. The changes in the fibrils and the plaques may appear at an early age. Lowenberg and Malamud [11] described Alzheimer's syndrome in a patient aged 24, and Hallervorden [15] reported typical changes in the fibrils in eleven cases of postencephalitic parkinsonism in patients between 11 and 50. A similar report was published by Fenyes,[16] of changes observed in a woman, aged 28. Hallervorden [15] found basket cells particularly frequent in his youngest patients, and this is an important observation in relation to chronological aging. We have to conclude, therefore, that the

13. Bozler, quoted by von Braunmühl.[12]

14. Rudzicka, quoted by von Braunmühl.[12]

15. Hallervorden, J.: Zur Pathogenese des postencephalitischen Parkinsonismus, Klin. Wchnschr. **12**:692, 1933.

16. Fenyes: Alzheimersche Veränderungen bei Parkinsonismus, Arch. f. Psychiat. **96**:700, 1932.

changes in the fibers are not necessarily the result of chronological aging but may be produced by a single etiologic agent. The same principles were applied by von Braunmühl [12] for the explanation of senile plaques, which he regarded as precipitations of tissue fluids.

These views accord with the clinical occurrence of Alzheimer's disease at different ages. In other words, similar physiologic changes may be produced by different factors, among which heredity may be of importance.

CONCLUSIONS

1. Alzheimer's disease may be subdivided into several clinical types: (*a*) the presenile type (hereditary transmission not known); (*b*) the intermediary type (with hereditary trends), and (*c*) the juvenile type (hereditary transmission not known).

2. Histopathologically, all the types mentioned constitute a unit.

EPILEPTIC CONVULSIONS AND THE PERSONALITY SETTING

OSKAR DIETHELM, M.D.
BALTIMORE

Much work has been done in recent years to clarify biochemical and neurologic factors in the vast and still confused field of "epileptic" disorders. The data observed, however valuable, have not yet been sufficient or adequately synthetized to explain convulsions. An important reason, no doubt, is the complexity of the factors involved and the fact that sufficient attempts have not been made to establish the interrelations with other biologic factors, and especially the setting in the whole psychobiologic unit—the personality. In studying an epileptic patient, one has to observe the type of integration which has been reached and the possible influence of part functions. This allows one to understand the influence not only of psychobiologic factors, but also of endocrinologic and other physiologic factors which are usually not analyzed but merely accepted (e. g., constipation and fatigue). Only in such a way will one be able to understand the factors which produce a convulsion and not mistake the incidental for the essential.

Even the clinical study of convulsive disorders is not yet sufficiently planned. What one actually ought to look for during a convulsion which one may have a chance to observe and what can possibly be investigated before and afterward are known only to a limited extent. There is too much tendency to work along one's own line of interest, which usually means a study of the factors of one part of the personality and a neglect of the interrelations.

Deplorable confusion has been caused by the exclusive emphasis on either psychogenic or organic factors. Hystero-epilepsy, affective epilepsy and psychasthenic attacks are frequently treated in the literature as if they were independent disease entities. The opposition of hysteria and epilepsy is the main issue in these discussions. Only a careful study of the personality and analysis of the symptoms and their setting allow one to understand these occasionally perplexing cases. The following case is a good illustration:

Case 1.—A woman, aged 35, had suffered from epileptic attacks (described as fainting attacks) since the age of 19. They occurred usually in a series of from three to four a day for a few days, with an interval of several weeks between. No biting of the tongue, frothing or incontinence was noted. When the patient was

From the Henry Phipps Psychiatric Clinic, Johns Hopkins Hospital.

27, facial palsy occurred on the left side, which lasted about a month; it recurred a year later and again at the age of 30, when the left arm and leg (rigidity and anesthesia) were also affected. The left optic disk was slightly pale and had an indistinct nasal border. The "fainting attacks" were more frequent during the periods of neurologic involvement. An exploratory craniotomy on the right side revealed a cerebral softening in the rolandic area. As the neurologic symptoms have now disappeared, except for a slight drooping of the right side of the mouth, it is justifiable to believe that they were manifestations of secondary postconvulsive lesions.

The patient had always been cheerful and easy-going, but also sensitive and excitable. At 22 she married a Protestant. Her mother, a devout Catholic, protested, and even more so when the children were brought up in the Protestant faith. The patient apparently grieved little until four years before the present report, when the mother became afflicted with cancer and blamed the illness on worry about her daughter. At that time the patient's attacks became more frequent and she had to enter the clinic, where she had from eighteen to twenty attacks a day, with few at night, for about a week—attacks of rigidity and jerking in the left arm and leg, usually with loss of consciousness and occasionally with only a dimming of consciousness. The attacks lasted for from one-half to two minutes, with a short space between. The head was frequently turned to the right; the pupils reacted to light; Babinski's sign was absent. At other times the patient was delirious for from one to several days. In these states she misidentified people and saw flowers, animals and colored lights. She often had fugues, which lasted from a few minutes to hours, in which she wandered about the city.

After her mother's death in May, 1931, the patient became increasingly depressed, and had more of the jacksonian-like attacks just described. In August there occurred brief delirious episodes in which she saw her mother, who had died without forgiving her for having abandoned her faith. In her hallucinations she heard the mother upbraiding her for having married a non-Catholic and for not having treated her well during her illness. When she was admitted to the clinic in the middle of August, she had from eighteen to forty convulsions a day in the form of violent clonic contractions, almost entirely confined to the right side (formerly they had been on the left). The pupils did not react to light at the height of the attack, but Babinski's sign was absent. At the end of such an attack the patient usually sat up, staring wild-eyed, clutching at the sheets, with an expression of terror, apparently experiencing a hallucination of her mother on her death bed, hearing her say that she (the patient) was going to hell. After about two minutes she slowly relaxed and was again in contact with the environment. When interfered with, the movements were frequently more purposeful rather than blindly resisting restraint. Occasionally there were rotatory movements of the head and rhythmic jerks of the flexed right arm. At other times the convulsions were more marked and generalized, involving both sides, occasionally with opisthotonos. The patient did not react favorably to large amounts of various anticonvulsive sedatives and psychotherapeutic reassurance. After about two weeks hypnotic reenforcement of reassurance was started. The patient was resistant to it, but responded well to an accordingly modified approach. The physician suggested that the picture of her mother would not appear any longer, not even in dreams, which had frequently disturbed her sleep. The patient improved in a few days, and fear, which had been her constant mood, was replaced by ease and contentment. The convulsions ceased within five days.

With the onset of hypnotic treatment, sedatives were entirely stopped. For a short period the patient was in as fair health as she had been two years before, having from one to two convulsions a month and a brief attack of fugue once in two months. She was more cheerful, although considerably concerned about an increasing retention difficulty, the beginning of which was noticed several years before. She was well adjusted to her mother's death and apparently no longer had remorse about her treatment of her mother and about her change of religion. I was able also to change her attitude of resentment and inadequacy concerning frigidity, which followed an operation for abdominal repair and dilatation and curettage for chronic endometritis in 1925. Since then, menstruation has been irregular and accompanied by a depressive and tense mood.

In this case there is no doubt that the disease is a progressive one with structural involvement. The successful psychotherapeutic approach dealt with only a phase of the illness, but an extremely distressing one, which I was otherwise unable to control. The temporary satisfactory state of the patient was primarily due to a better personality adjustment, maintained by discussing with her the minor difficulties of the day. Anticonvulsive medication is important to prevent further damage to a highly susceptible brain. Advice was given with regard to general hygiene and diet. There are no indications for any specific treatment.

The convulsive seizures in this patient are not of the usual epileptic type, but one must be willing to accept marked individual variations in a field in which the whole personality is involved. There has been a remarkable stereotypy of the convulsions since 1925, with no essential change of the symptoms, but only an increase under emotional strain.

It would be wrong to speak here of hysterical tendencies. Essential in hysteria is the dissociative-dysmnesic substitution character, and nothing in this case proves that these factors are predominantly at work. The increase of epileptic symptoms during emotional stress is a common phenomenon and does not necessitate a special classification (e. g., "affect epilepsy").

Somewhat surprising was the observation that one of the convulsions was stopped by hypnosis. (The convulsion started just after the patient had been put in a hypnotic state.) Even such an occurrence does not point to a hysterical nature, but indicates the far-reaching possibilities of suggestion in this person. In each epileptic convulsion one has to deal with psychologic as well as with humoral, circulatory, neurologic and other obviously organic features. Personality factors, such as suggestibility or affective features, play a varying rôle according to the individual patient, changing in each according to the whole personality setting at the time of the actual occurrence of the convulsion. It is therefore occasionally possible to influence the course of an attack by suggestion. The case of a child who had convulsions following encephalitis may serve as an illustration.

CASE 2.—A boy, aged 16, who had been spoiled and had presented behavior difficulties since infancy, had "flu" and encephalitis in 1922 (at 7 years). Shortly afterward he began to have attacks characterized by sudden onset, with loss of consciousness, a tonic phase of a few seconds, followed by a left-sided convulsion, with the pupils rigid to light, but without loss of sphincter control or biting of the tongue. He had occasionally an aura ("a peculiar feeling in the eyes"). These convulsions have been present for nine years. Occasionally they have been more generalized. Shortly after their onset left hemiparesis developed, which disappeared after a month. About one year later, parkinsonian symptoms appeared, increasing steadily. At present there is marked rigidity of the arms and legs, with hyperactive tendon reflexes and a positive Romberg sign, a masklike face, indistinct speech, occasional drooling of saliva and slight weakness of the left side. His adjustment on a farm was difficult because of temper tantrums, mischievousness and unwillingness to accept discipline. During times of more behavior difficulties the convulsions increased in number (from ten to twenty a day), but there was always considerable improvement when he was admitted to the Phipps Clinic, where he adjusted fairly well to the regimen. It was noticed frequently that the convulsions seemed to be provoked by emotional excitement, and hypnotic investigations were therefore undertaken during the first admission at the age of 11 years. After considerable resistance, deep hypnosis (with catalepsy and amnesia) was reached. It was possible afterward to stop several convulsions by suggestion. One attack was stopped at the beginning of the tonic phase; another was stopped at the end of this phase, and several at the beginning of the clonic phase. The patient disliked the hypnotic treatment considerably and frequently had attacks at the beginning of hypnosis. It was possible to stop these convulsions through suggestions as soon as the first signs were noticeable and to proceed undisturbed with the hypnosis. Several times hypnotic suggestions failed to influence the attacks. After about three weeks the procedure was abandoned because no lasting therapeutic gain was obtained.

As in the previous case, the patient was submissive and suggestible. It is therefore not surprising not only that education and suggestions favorably influenced the general behavior, but also that the convulsions diminished greatly and the neurologic symptoms became somewhat less marked. This does not prove more than the dependence of neurologic and convulsive symptoms on psychologic factors, and does not argue for a psychologic etiology. Besides definite postencephalitic structural and functional changes, constitutional factors may play a considerable rôle in this case. A maternal great-aunt had epilepsy. The left hemiparesis and subsequent weakness might be explained by a secondary lesion.

SUGGESTIBILITY

This case cautions one not to consider the fact that a convulsion can be provoked in hypnosis, or under other suggestive influences, as proof of its hysterical nature. The possibility exists that an epileptic convulsion might be started by the physician through a marked emotional upheaval (e. g., the fear of the hypnosis in the first case) at a time when there is a marked readiness for attacks. Autosuggestion does not

seem to play a rôle. It is probably the direct influence of strong emotions. The emotions which caused the convulsions at the beginning of the hypnosis, to which the patient did not wish to surrender, are closely connected with the opposition to the hypnotic approach. This case shows excellently the interrelations of emotions and suggestibility. With this I do not wish to accept completely Bleuler's theory [1] that suggestions have to be of an affective nature and that suggestibility is a part of affectivity. Suggestibility is an important personality feature which has not been sufficiently studied. The average epileptic patient is apparently not very suggestible, but marked individual differences exist. Owing to the still lingering influence of Babinski,[2] many psychiatrists have a tendency to consider suggestibility and the possibility of influencing symptoms by hypnosis as evidence of hysteria.

Only in a few cases with epileptic convulsions is one able to secure psychologic material which is of importance, at least as a precipitating factor. Hypnotic investigations of petit mal attacks and epileptic fugues gave similar findings. They revealed that consciousness is fluctuating. There was only a brief period which the patients were unable to reproduce. This must correspond to a really unconscious state, best compared to coma. Reexperiencing the other part of the so-called unconscious period, the patients were usually able to give a more or less vague appreciation of surrounding objects. Not dependent on the fluctuations of consciousness were bodily sensations of varying intensity, localized especially in the throat and face and less frequently in the hands and neck. There was always a marked concentric constriction of the visual field. (Other authors have noticed a postconvulsive concentric restriction which may last some time.) The content is pictorial and apparently remarkably monotonous, dealing with objects of the surroundings or of daily life. Even in these typical cases of petit mal attacks in which careful study had not revealed special problems to be of dynamic importance personality factors frequenlty colored the content. In one case the fiancée's picture appeared, and especially parts of the room in which he had proposed several years previously. This patient was trying to decide about terminating his engagement because of his epileptic illness, but at no time did one have the impression that this problem was influencing the frequency of the attacks.

These findings warn one not to evaluate too hastily concentric constriction of the visual field or unusual sensory disturbances as conversion symptoms. It is also desirable not to interpret the various parts of a convulsion from a symbolic point of view. There is no doubt that unusual features in an attack can be symbolic expression (some might

1. Bleuler, P. E.: Affectivity, Suggestibility, Paranoia, Utica, N. Y., State Hospital Press, 1912.

2. Babinski, J.: Exposé des travaux scientifiques, Paris, Masson & Cie, 1913.

feel justified to use such an explanation in case 3), but the usual convulsion is automatic and therefore monotonous in its form.

In recent years the importance of personality factors influencing seizures has been increasingly emphasized, as is well seen in Notkin's[3] discussion of the literature. This author, and especially Cobb,[4] stressed the need for considering the emotional element at least as a precipitating factor in bringing about a convulsion. This is further elaborated by Fremont-Smith,[5] who distinguished between organic disease as the predisposing and emotional tension as the precipitating factor.

It is important to realize the possibility of personality factors influencing the form of symptoms which one is usually willing to explain entirely by lesions of the brain.

Case 3.—A woman, aged 46, suffered from multiple sclerosis. The first symptoms of the illness were petit mal attacks which appeared when she was about 39. She became slightly depressed about this and about the development of reactions of the type of epilepsia procursiva. (This was apparently automatic, and fear was not a factor.) Noticing double vision, she had an increased fear of insanity. Since then (for six years) she had had frequent attacks of loss of consciousness, frothing and slight tonic convulsion. She often had an attack of stupor lasting from two to four hours. In both conditions she had Babinski's sign on both sides, but the pupils reacted to light. At other times she had fuguelike attacks of walking about, with automatic movements and amnesia. During one year of observation her condition grew worse. The stuporous attacks increased and showed occasional interesting variations. During one such attack she was thrashing around in the bed, pounding with her right fist and at times showing rather suggestively erotic movements of the abdomen and legs. During this attack she seemed conscious; the pupils reacted well to light, but there were suggested Babinski sign and amnesia for the whole episode. Similar erotic behavior in these attacks had been noticed by the husband. It seemed to have started two years previously, after she had been analyzed by a physician who pointed out to her sexual factors as the most important. Such obviously erotic behavior was an unusual feature in this reserved, shy, gentle, highly sensitive woman.

One might think of the possibility of stirring up latent sexual desires and an erotic coloring of an otherwise organic attack. There is no justifiable reason to connect it with any localized lesion of the brain. Too little is known about this. The erotic behavior with lesions of the frontal lobe, for example, is probably due to a disturbance in inhibition. The frequent erotic behavior of epileptic patients is apparently more complex. It is probably due more to personality changes, although lack of judgment and restraint of impulses may be contributing factors.

3. Notkin, J.: "Affect Epilepsy" and "Hysteroepilepsy": Study of Convulsive States in Psychopaths, J. Nerv. & Ment. Dis. **72**:185 (Aug.), 226 (Sept.) 1930.

4. Cobb, S.: Causes of Epilepsy, Arch. Neurol. & Psychiat. **27**:1247 (May) 1932.

5. Fremont-Smith, F.: Influence of Emotion in Precipitating Convulsions, Arch. Neurol. & Psychiat. **30**:234 (July) 1933.

Whether the epileptic constitution is characterized by sexual excitability is a disputed question. Besides organic (structural) factors, the constitutional disposition to convulsions must be considered in this case. A brother died of epilepsy, and a sister suffers from nausea and dizziness.

Similar personality factors can be noticed in cases of tumor of the brain and often obscure the neurologic picture.

CASE 4.—A patient, who died of a malignant tumor of the ethmoid, presented as the outstanding symptom attacks of stertorous breathing. After about one minute he kept his breath back until he became darkly cyanotic, when the body began to extend into a rigid arch. After a few seconds he again began to breathe fast, but the arching continued for several minutes. These attacks repeated themselves during periods of from ten minutes to two hours and were brought on by excitement. He was difficult to manage because of his irritability and stubbornness. These features were exaggerations of tendencies of his normal make-up. By teaching the patient to breathe deeply and quietly, especially when laborious breathing started, and by suggestions, it was possible to diminish the attacks temporarily, despite the continuous growth of the tumor.

Case 4 not only illustrates the influence of psychotherapy on personality determined features, which in this case are merely incidental, but brings up the question of the nature of the attacks. Not enough was elicited to explain the attacks as psychogenic, but the patient's constitutional make-up and psychopathic heredity factors probably presented the material which was utilized by the structural damage to the brain, although the possibility of localized disturbance, due to the growth of the tumor, cannot be excluded as no autopsy was obtained. That the patient is influenced by suggestion or by another psychotherapeutic approach does not prove the psychogenic origin of a symptom or a group of symptoms. The constant hiccup of a patient suffering from a cerebellar tumor stopped while he was under slight hypnosis, but there was no doubt about the central origin of the symptom. The hypnosis caused temporary relaxation and ease which had been disturbed in this man by a hold-up a few weeks before admission, after which the symptoms of ataxia and hiccup became obvious.

These cases with an undoubted structural basis support the claim that psychotherapeutic success with epileptic symptoms does not argue for the need of establishing a new entity. With increasing understanding of the various factors—of what is neurologic, organogenic, exogenic, constitutional or psychogenic, and the interrelations of these factors and their influence on the whole integrated personality—one will be able to form new groups among the large group of epileptic disorders. The approach which stresses phychologic features to the extent of using them in contrast and often in superordination to all other factors neglects to consider the personality as a psychobiologic unit.

It is possible that the same disposition forms the soil for epileptic attacks in one person and for hysterical convulsions in another, but this is a mere hypothesis and needs careful investigation and proof. One may observe hysterical attacks with definite involvement of the neurologic level, but this is no more at the present time than an illustration of far-reaching psychobiologic influence. I observed a young woman with attacks of hysterical stupor in which the pupils did not react to light, and in which, at least once, the corneal reflexes were absent. The patient recovered completely.

It is not justifiable to speak of hysterical features when one wants to indicate merely psychobiologic influences and reactions and not definite dissociative-dysmnesic substitution phenomena. The concept of hysteria should also not be broadened to such an extent that it means simply "psychogenic." Epileptic and hysterical attacks may occur at various times in the same patient, but this seems to be rare. Much of the older literature on this topic needs critical review. What I wish to warn against is the assumption that mixed forms of hysterical and epileptic convulsions are common. Notkin's [3] theory of the "possibility of an hysterical manifestation transforming itself into a more severe organic reaction of an epileptic nature" is alluring, but needs careful study and analysis of suitable cases to be substantiated. It is possible that it will lead to a singling out of specific personality reactions.

EMOTIONAL FACTORS

Emotional factors always deserve careful evaluation. The influence of minor reactive moods on convulsions is well known. Anticipation of excitement is frequently stronger than actual experience. Few convulsions are observed while the patient's attention is fully absorbed in such a situation. Fear produces unusual types of attacks in nonepileptic persons, but it can also cause characteristic epileptic convulsions, especially in poorly organized persons.

More lasting changes of mood are less frequently observed in epileptic patients, but they are possible, as in other persons with a constitutional tendency to them, and may cause an increase of convulsions. Case 1 illustrates well this possibility and the influence of such situationally determined depressions. The patient had a constitutional tendency to depressions. (Her mother had a depression and her father's and a brother's heavy alcoholism was partly on the basis of emotional maladjustment.) Another marked depressive mood swing recently necessitated hospitalization again. These reactions are different from the increasing emotional instability which accompanies progressive epileptic disorders. The latter are part of the epileptic illness. Other patients

show a more euphoric mood or the impure mood of tension and irritability. The adjustment of these emotional difficulties is important, as it diminishes convulsive reactions. These symptoms are frequently the expression of a too easily or too intensely reacting person, but seem also to occur as an automatic symptom. How much endocrinologic factors play a rôle, as in the disturbance of mood in the menstrual period, is not clear. The relation to definite affective psychoses, depression and manic excitements has not been clarified sufficiently, although it has caused considerable discussion.

There is no reason why constitutional tendencies to affective reaction could not exist in an epileptic person. One finds, therefore, various types of affective psychoses. More difficult to explain are cases like the one of an epileptic person, aged 25, who had a hypomanic reaction at 17 and a depression at 21, which lasted several months and was of an unusual type. It terminated within a few days after the patient had a series of four convulsions. This man's convulsions started at 18 and have persisted since except for the period of the depression. It is well known that epileptic irritability and moodiness are relieved by attacks, but the termination of a marked affective psychosis is unusual.

The term "affective epilepsy" is not good, for it stresses unnecessarily and exclusively the well known influence of emotional factors on convulsions. It is not surprising to find these reactions, especially among certain psychopathic persons of the emotionally excitable, poorly controlled group.

PERSONALITY ORGANIZATION

The organization of the personality and its relations to convulsions deserve much attention. One is impressed by the frequency of various types of convulsions in psychopathic persons, i. e., those who are constitutionally poorly integrated personalities. Oppenheim spoke of "psychasthenic attacks." Only clear descriptions, with investigations of all the factors involved, will allow one to decide whether some of these attacks ought to be separated from epileptic convulsions. Owing to insufficient organization of the personality, motor reactions seem to occur more easily in psychopathic than in well organized persons. This explains also the frequency of motor neuroses (tic, torticollis) in such a setting and resistance of the patients to complete adjustment, while at the same time they seem to be temporarily well influenced by psychotherapy. A loosening of personality organization during menstruation causes manifold symptoms, among them an increase in epileptic symptoms. Symptoms which are entirely or partly due to insufficient organization in childhood and adolescence become less marked or disappear with maturity.

Fugues are frequently observed in the poorly organized psychopathic personality, without necessarily indicating an epileptic illness. Attacks of fugue are interesting phenomena. They seem to be more closely related to the psychobiologic level than the other more automatic epileptic features. Epileptic fugues lend themselves well to hypnotic investigations, but differ apparently from hysterical fugues by offering only an incomplete reproduction under hypnosis. In my cases I always came to several phases which I was not able to elucidate. They apparently correspond to states in fugues in which the patient is motionless and in a deeper state of unconsciousness than at the times of more or less coordinate activity. No special content was obtained. Nevertheless, the fact seems to remain that fugues occur in persons with actual life difficulties. Fugues again are frequently observed in the poorly organized psychopathic person.

The observation of fugue and delirious twilight states without convulsions leads to the concept of "epileptoid psychopath," a term which fortunately has already begun to disappear from psychiatric literature. It blurs the none too clear delimitation of what is meant by epilepsy and adds too many psychopathic characteristics to the epileptic constitution.

The question of the epileptic constitution is still open to discussion. Studies of heredity have not clarified the point. Observations like mine of three epileptic families (in two of which two siblings, and in the third the father and two children, suffered from epileptic convulsions and petit mal attacks) argue for hereditary factors. In these, as well as in other families with only one epileptic member, one finds that siblings as well as one of the parents and even the grandparents had similar personality traits without any manifestations of epilepsy. These characteristics can be noticed in adults and children. These children are frequently slow in grasping, but do well when given sufficient time. In execution they are inclined to get lost in details. Conscientiousness may exaggerate this intellectual trait. Because of these features and a tendency to day-dreaming, good educational results can be obtained only by adapting the teaching method to the child. Well known features are also epileptic sensitiveness, egocentricity, irritability, stubbornness and persistence in actions as well as mood, which make adjustment to the group difficult.

In all these cases one has to consider the possibility of preconvulsive and postconvulsive personality reactions and the reactions of a child to the illness and its handicaps. The aforementioned intellectual features could not be explained by such factors, and argue more for definite constitutional peculiarities, especially as I have noticed them also in

some healthy members of the family. Such observations cannot be explained as an early symptom of epilepsy. "Latent epilepsy," which has been used as an explanation for these features, is a term which is best avoided. Studies of the physical make-up of such families might further clarify the question of the epileptic constitution.

It is possible that cases of epilepsy with a history of that disease in several members of the family form a unit in the group of epilepsies and follow their own hereditary laws. Symptoms of essential deterioration are not always found in such cases.

Although the clinical picture of epileptic deterioration is well known, it is impossible to determine at present what is essential and what is more incidental, in the sense of habit deterioration. Cobb [6] stressed this in discussing whether deterioration is an effect of repeated convulsions and drugs, or whether it is really a part of the epileptic syndrome. The influence of drugs has been greatly exaggerated in the past. On the other hand, the findings of Gärtner [7] and others urge reconsideration of this factor in permanent deterioration. One cannot say yet whether the retention and memory disorders are always present in connection with secondary lesions or whether they may occur with a primary process which does not necessarily need to be a structural disorder of the brain. What A. Meyer [8] proposed for the study of habit deterioration in schizophrenia might well be remembered in an approach to the problem of epilepsy:

> . . . to study the working of the various sets of activities and habits in the patient, determine their relative values by accurate observation coming up to the mark of the experiment, and shaping out therapeutic measures in accord with these principles. This naturally does not exclude in any possible way the consideration of the factors of heredity, and the disorders of this or that organ, but, on the contrary, gives every manageable part its working chance.

For a thorough adjustment, therefore, environmental factors must also be considered. The patient's attitude to his illness and to life is frequently unfortunate. It is a mixture of carelessness with regard to the dangers to which he is subjected by his convulsions and overconcern for minor ailments or discomforts. Few patients have a hypochondriac attitude toward their convulsions, but rather that of being annoyed or discontented. The aim is to make a patient live with his symptoms in

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6. Lennox, W. G., and Cobb, S.: Epilepsy, Baltimore, Williams & Wilkins Company, 1928.

7. Gärtner, cited by Lennox and Cobb.[6]

8. Meyer, A.: The Rôle of Habit Disorganization in the Essential Deteriorations (Dementia Praecox) and the Relation of the Deterioration Process to the Hysterical, Neurasthenic and Psychasthenic Constitutions, Nervous and Mental Disease Monograph Series no. 9, 1912, p. 95.

the best possible and most normal way; not to stress these handicaps too much, but to accept them as worthy of careful treatment. In the work adjustment the present mental status of the patient must be carefully considered, and possibly an adjustment on a lower working level attempted. The fact that it is still not clear how much of the frequently progressive intellectual impairment is due to primary or secondary lesions, to drugs or poor management, or to a special type of habit deterioration must be kept in mind. The grouping of epilepsy in psychiatric classifications shows this clearly, as some consider it under structural disorders (organic psychoses) while others discuss it under psychoneuroses.

It is not necessary that convulsions in the setting of cerebral arteriosclerosis or structural disorders of the brain be directly due to a neurogenic disorder. These illnesses disturb the personality organization and its regulative factors. A constitutional predisposition to convulsive reactions may become manifest. Many cases of alcoholic epilepsy must be explained on such a basis.

The possibility of the appearance of convulsions due to disorganization of the personality has not yet been clarified. Epileptiform attacks in schizophrenic reactions are rare and have not been sufficiently studied. It may be that there is only an apparent similarity to epileptic convulsions, but also that such attacks may occur in a disorganized personality while they were not possible when the same personality was still well integrated. From this point of view the constitutionally nonorganized person ought to be compared with the disorganized personality. There is still a strong tendency to force all these attacks into one entity instead of speaking frankly of a convulsion or a comatose attack in a catatonic illness or in a marked fear reaction—to point out two of their most frequent settings. A carefully planned observation with an investigation of the various possible aspects will show in what ways these attacks are similar to some of the epileptic convulsions. It is possible that vasomotor disturbances and hyperventilation are important factors. On the other hand, one needs a certain constellation of these and other factors to allow a constitutionally predisposed brain to react with a convulsion.

CONCLUSIONS

In studying epileptic patients the whole personality must be considered, with attention to all factors and their interrelations. It is essential to distinguish the merely incidental from the leading features. Some characteristic personality features seem to be constitutional (at least in a certain group), as they are found in other members of the family without epileptic manifestations. Epileptic seizures of various types are open to the influence of psychodynamic factors.

Affective and topical material may appear. One must be careful not to use the term "hysterical" for all of these psychodynamic factors. Hypnotic investigations of epileptic as well as of organic disorders of the brain show the possibility of personality involvements. The mere appearance of these features is, therefore, not the issue; their evaluation in the whole personality setting and the direction of the therapeutic approach are the important thing. In this presentation I have tried to clarify the problem by an analysis of suggestibility, emotional tendencies and personality organization.

THE RED NUCLEUS

ITS RELATION TO POSTURAL TONUS AND RIGHTING REACTIONS

W. R. INGRAM, PH.D.

S. W. RANSON, M.D.

AND

R. W. BARRIS, M.S.

CHICAGO

The mechanism of the regulation of muscle tonus has constituted a long and absorbing, although as yet uncompleted, chapter in the study of functional neurology. Recently, a certain school of investigation, now led by Rademaker, designated the nucleus ruber as the chief center for the regulation of muscle tonus, and in support of this idea, Rademaker[1] presented data from a series of experiments in which the decussation of Forel was sectioned in thalamic animals and the red nuclei were directly destroyed by gross lesions in otherwise intact animals. These operative procedures were said to produce rigidity of a high degree and also to interfere with the execution of certain of the normal body righting reactions. The red nuclei were considered not only as tonus-controlling centers but also as centers for the mediation of labyrinthine righting reactions and of body righting reactions acting on the body. Body righting reactions acting on the head were believed to be carried out by some adjacent portion of the mesencephalic tegmentum but not by the nucleus ruber. This work has been criticized by various authorities on the grounds of the possible involvement of other important structures by the lesions, which were rather extensive. These criticisms, as well as the general aspects of the problem, were considered in some detail in previous publications by two of us (W. R. I. and S. W. R.[2]), in which were reported the results of a series of acute and chronic experiments with cats in which the red nuclei were destroyed bilaterally by restricted lesions. After the production of such lesions, it was observed that the animals were able to right themselves, and stand and walk, even after the visual righting reflexes had been eliminated. The gait was

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From the Institute of Neurology, Northwestern University Medical School.

1. Rademaker, G. G. J.: Die Bedeutung der roten Kerne und des übrigen Mittelhirns für Muskeltonus, Körperstellung und Labyrinthreflexe, Berlin, Julius Springer, 1926.

2. Ingram, W. R., and Ranson, S. W.: Effects of Lesions in the Red Nuclei in Cats, Arch. Neurol. & Psychiat. **28**:483 (Sept.) 1932; The Place of the Red Nucleus in the Postural Complex, Am. J. Physiol. **102**:466, 1932.

marked by ataxia, dysmetria and transient loss of position sense of the limbs, and while there was a mild increase in the tonus of the extensor muscles, it was not sufficiently pronounced to interfere greatly with the activities of the animal.

At this time a careful study of labyrinthine and body righting reactions in such animals was not made, and it has been thought desirable to carry out further experiments in an attempt to observe the effect of this operation on such reflexes and to reexamine the results already reported. It was also thought that in certain features the behavior of animals without the red nuclei resembled that of decerebellate animals, as described by Rademaker [3] in his fine study of postural reflexes, and that an attempt should be made to determine if certain of the symptoms observed might possibly be due to impairment of cerebellar functions, since the red nucleus is an important station on the chief efferent pathway of the cerebellum. This has been done by observation of certain postural reactions which have been analyzed and described by Rademaker with special reference to their manifestation in decerebellate animals.

MATERIAL AND METHODS

These experiments were carried out on a new series of cats in which lesions had been produced in the red nuclei with the aid of the Horsley-Clarke stereotaxic instrument. The technic involved has been described in detail elsewhere.[2a] All the experiments were of the chronic type in which the operations were performed under aseptic conditions and the animals were kept a sufficient time for observation, in some cases as long as four months. In this series there were twenty animals, including five in which destruction of the red nuclei was patently incomplete, seven in which it was almost or practically complete and eight in which it was complete. The extent of damage to the red nuclei was determined by a study of microscopic sections of the brain stems, stained by the Weil and cresyl violet technics. The former stain, being specific for myelinated fibers, was useful in ascertaining the amount of damage to the decussation of Forel or to the rubrospinal tract in cases in which the red nuclei themselves were not completely destroyed. The cresyl violet stain was especially useful in instances in which the time of survival had been sufficient for degeneration of any red nucleus cells not directly affected by the lesion, but the axons of which might have been severed, giving an index of the number of surviving functional cells.

A number of these animals and a group of three normal cats were subjected to bilateral destruction of the labyrinths. This was carried out by application of the technic of de Kleyn (Magnus [4]), which gives a bloodless field. It was possible to see the vestibule, cochlea and ampullae as they were exposed and removed, and finally the eighth nerve where it lay exposed in the internal auditory meatus.

To eliminate confusion due to visual righting reflexes, the other righting reactions were studied in blindfolded animals, for which purpose a special head mask of leather was devised. With the mask in place, the labyrinthine righting reflexes

3. Rademaker, G. G. J.: Das Stehen, Berlin, Julius Springer, 1931.
4. Magnus, R.: Körperstellung, Berlin, Julius Springer, 1924.

were tested by immersing the animal in water or by dropping it from an inverted position, allowing it to fall into a net. The body-on-the-body righting reactions were determined by laying the animal on its side, holding the head firmly with one ear against the table top and noting if the body was then brought into an upright position. The body-on-the-head righting reactions were observed in a labyrinthless animal by laying it on its side and noting if the head was then brought into an upright position.

Changes in the muscle tonus of the limbs were studied when the animal was supine, or when it was suspended in an upright position in a canvas hammock in which there were holes through which the legs hung free. Under these conditions comparatively slight changes in tone can be determined by noting the amount of resistance to passive flexion of the limb and to pressure applied to the pads of the feet in such a manner as to elicit the positive *Stütz* reflex. The former method is especially suitable for estimating the degree of tonus of the extensor muscles, while the latter applies also to the amount of *Stütz* or standing tone of the limb as a whole, in which the flexor muscles may play a supporting rôle. Alterations in muscle tonus which might not otherwise be noticed may be brought out when the animals are studied under the foregoing conditions.

OBSERVATIONS

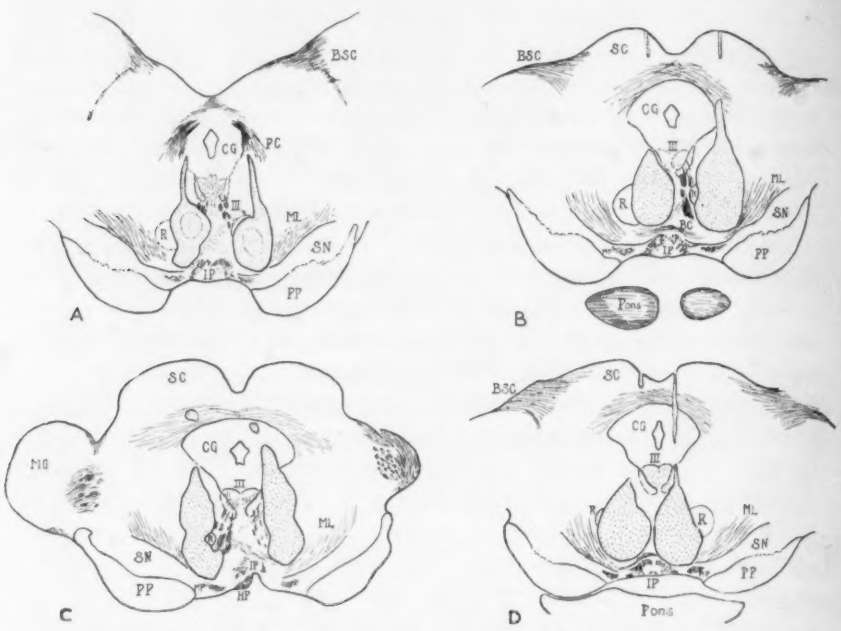
Observations of the general behavior and gait of the cats of this series in which the red nuclei or their descending connections were completely or practically completely destroyed confirm the observations previously reported. The gait is characteristic. In the early stages it is marked by considerable ataxia and incoordination, together with diminished position sense of the limbs, because of which the toes are turned under and the weight is frequently thrown on the dorsum of the foot. After a few days this usually disappears, and better coordination is secured. There is a marked tendency to overstep, especially affecting the forelimbs, which are lifted high and extended far forward. The hindlimbs assume a wide base and are circumducted when moved forward, and at the end of the step a sort of skating movement is executed in which the foot is slid forward and outward along the floor; there is also a definite impression of stiffness in the hindlimbs. Frequently these cats show rocking or a to-and-fro rotation of the pelvis when walking. There may be some amelioration of these phenomena in the course of time, but even after a lapse of several months the gait is quite striking and readily distinguishable from that of a normal animal. Judging from Rademaker's description, these abnormalities are similar to those occurring in walking, decerebellate cats, although probably emphasized to a lesser degree, as there does not seem to be the extraordinary amount of zig-zagging and irregular lateropulsive movement implied by Rademaker's account.

Tonus Reactions.—There is a tendency to increased tonus of the extensor muscles, which is not great enough to interfere with locomotion, although sometimes apparent in the animal's standing position, but

which is manifest under the conditions already mentioned. When the cat is suspended with the limbs hanging free, there is increased resistance to passive flexion of the limbs and marked resistance to pressure on the pads of the feet, and there are usually "following" *Stütz* reactions, probably proprioceptive, in which the limb will follow the hand into an extended position. Satisfactory magnet or exteroceptive *Stütz* reactions were difficult to elicit and were rarely seen in our cats. The increase in tonus was also evident when the animal was supine. Normal cats under the same circumstances give poor responses, such reactions as are obtained being complicated by escape and avoidance movements in which flexion of the limbs plays a large part. There is evidence, also, that pressure on the dorsal surface of the body may inhibit the *Stütz* reaction in normal animals. The prominence of the tonus reactions when the cat is on its back furnishes a further point of resemblance to the situation in decerebellate animals, in which the normal inhibitory effect of pressure on the skin of the back is not manifest. In the course of time, these tonus reactions become somewhat less marked.

Righting Reactions.—As previously reported, these cats are able to right themselves and maintain an upright posture when on a supporting surface, although in some cases this may be interfered with by the occurrence of forced movements which cause a twisting or lateral bending of the neck and trunk. These forced movements are not infrequently observed in animals with lesions of the tegmentum, especially if the damage is greater on one side of the midline than on the other. In the present series the movements that occurred were not severe enough to complicate the results. That the righting ability just mentioned cannot be due entirely to visual righting reflexes is shown by the fact that blindfolding or enucleation of the eyes does not affect it. The other righting reflexes concerned could be determined only by specific examination, and, therefore, six cats with practically complete destruction of the red nuclei were tested for the occurrence of labyrinthine and body-on-the-body righting reactions according to the methods outlined. In one of these cats the red nuclei were completely destroyed, while in the others possibly a few cells on one side may have escaped. When blindfolded and dropped from an inverted position all the cats were able to right themselves. Two of them were placed in water and were able to maintain an upright position. Thus, the labyrinthine righting reactions may be said to have remained intact. The same animals, laid on their sides with the head held firmly so that one ear was against the table, demonstrated the integrity of the body-on-the-body righting reaction by bringing the trunk into an upright position. *A* in the illustration shows typical lesions in this group of animals.

The body righting reactions acting on the head can be tested only in labyrinthectomized animals, and since such an operative procedure would furnish a further check on the validity of the labyrinthine righting reactions previously obtained, six cats were deprived of their labyrinths several months after destruction of the red nuclei. Each of these animals displayed the disturbances typical of labyrinthless cats in the acute state, such as irregular excursions of the head, violent threshing motions of the limbs and disorientation when attempting to walk. They lay with the ventral side of the body resting on the floor. In one cat



A, cross-section of the brain stem of cat 35, showing the extent of the lesions. The portion of the left red nucleus which lies outside the lesion is practically completely degenerated; a few normal cells remain in the right red nucleus. *B*, cross-section of the brain stem of cat 39, showing the extent of the lesions. The portion of the left red nucleus which lies outside the lesion is completely degenerated; the right contains a few normal cells. *C*, cross-section of the brain stem of cat 43, showing the extent of the lesions. The right red nucleus is completely degenerated; the left possibly contains a few normal cells. *D*, cross-section of the brain stem of cat 30, in which the labyrinths had been destroyed some time before the operation for rubrectomy. The areas ordinarily occupied by the red nuclei show degeneration. The following abbreviations are used: *BC*, brachium conjunctivum; *BSC*, brachium of the superior colliculus; *CG*, central gray matter; *HP*, habenulopeduncular tract; *IP*, interpeduncular nucleus; *MG*, medial geniculate body; *ML*, medial lemniscus; *MP*, mamillary peduncle; *PC*, posterior commissure; *PP*, pes pedunculi; *R*, nucleus ruber; *SC*, superior colliculus; *SN*, substantia nigra, and *III*, third nerve and oculomotor nucleus.

persistent weakness and the development of infection prevented recovery to a degree sufficient to make righting of the trunk possible. In five of these cats the visual and body righting reactions were obviously present, but in three of them further analysis was prevented by the occurrence of an epidemic of distemper. *C* shows the lesions in one of these cats. Two of them made good recoveries, however, and it was definitely shown that the body-on-the-body and body-on-the-head righting reactions were present in these animals after the visual reflexes had been eliminated by blindfolding. In one of the cats, 39 (*B*), the red nuclei were destroyed except for a few scattered cells on the right side, and the lesions were so placed that it was difficult to see how any crossed descending connections could have remained. In the other cat, 41, the lesions apparently severed the decussation of Forel, destroying the right red nucleus and all but a few cells of the left.

The converse of this group of experiments was also carried out. Three cats in which both labyrinths had been destroyed four months previously were operated on for destruction of the red nuclei. These animals had originally shown all the usual symptoms of labyrinthine deficiency and had attained a good degree of compensation so that they were able to get about and care for themselves in good fashion. The excursions of the head had practically disappeared; the cats maintained their equilibrium well and were able to support their bodies clear of the floor and to walk, although in rather a jerky, hesitant manner. The abrupt, excursive movements and nystagmus of the head were emphasized only in periods of excitement or stress. In two of these animals the red nuclei were completely destroyed; in the other, the destruction was almost complete, as shown by subsequent microscopic examination at autopsy. In one of the former the lesion was greatly extended by the development of an area of softening, and there was not a good recovery from the operation; a strong forced movement developed in which the spinal column was curved concavely to the right, and the cat was able to right itself from the left side only. The *Stütz* and tonus reactions were markedly increased, and the limbs were capable of supporting the weight of the body. The ability of the cat to balance itself when standing was lost, owing largely to the forced movement. The other two cats, however, retained the body righting reactions, manifested disorders of gait which closely resembled those described by Rademaker for decerebellate animals and showed increases in the *Stütz* and tonus reactions. Cat 28, when blindfolded, stood with a wide base of the limbs and its neck retracted and maintained an upright position. The labyrinthine righting reactions were absent. Body-on-the-head and body-on-the-body righting reactions were positive and took place with great celerity. In this animal, the right red nucleus was partly destroyed, and all of its crossed descending connections were severed.

The left nucleus was also partly destroyed, but while the majority of its efferent fibers were cut off by the lesions, a number escaped, as shown by the presence in it of some normal cells at one level. Cat 30 showed some signs of catalepsy and forced movement after the second operation, which accentuated a naturally quiescent attitude. When blindfolded, it could maintain an upright position when quiet, but on attempting to move it sometimes fell to the left as a consequence of the forced movement. The labyrinthine righting reactions were absent. The body-on-the-head righting reaction was poor, but positive. The body-on-the-body was delayed, but positive. The naturally timid disposition of the animal, not improved by blindfolding, complicated the execution of these tests, but no doubt could be had as to their validity. At the time this animal was killed it showed ability to make some progress in the usual ataxic manner. Autopsy showed the red nuclei to be largely destroyed, the portions that were left being filled with degenerated cells. Only a few scattered cells of normal appearance were found on the right side. *D* in the illustration shows the lesions in this case.

In general, the chief result in these experiments was a superposition of the effects of one operation on those of the other, with, in certain instances, enhancement of some of the abnormalities. In this connection it seemed that the chronic labyrinthless cats showed more bizarre disorders of gait after destruction of the red nuclei than did normal cats, so that they more closely resembled decerebellate animals. It might then be suggested that the extreme disturbance of gait in the latter type may be due in part to some involvement of the vestibular apparatus accompanying removal of the cerebellum.

Postural Reactions.—Efforts to find still other means of comparing cats without the red nucleus to decerebellate animals led to the examination of certain of the postural reflexes. A detailed study of the complex reactions involved in the maintenance of normal posture and the adaptation of the limbs and body to various orientations of the supporting surface has been reported by Rademaker.[3] Certain of these reactions seem to be abnormal in chronic decerebellate animals, and may display exaggeration, delay, or hypermetria. Therefore, some of the reactions were tested in our "rubrectomized" cats and compared with those of normal animals, Rademaker's description of the same phenomena in decerebellate animals being taken into account.

1. The first of these reactions to be examined was the effect of raising and lowering the head on the *Stütz* tonus of the hindlimbs. According to Rademaker, passive lowering of the head in dogs and cats causes sharp extension of the hindlimbs, whereas raising the head causes diminution of the *Stütz* tonus of those members. Apparently

such reactions are readily demonstrable in dogs, and seem to be especially strong and striking in the chronic stages following removal of the cerebellum. Owing to the temperamental peculiarities of cats, however, demonstration of the reactions in these animals may be difficult, and in our experience no positive effect could be secured in ten of eleven normal animals. Similar negative results were obtained in six cats in which there was practically complete destruction of the descending rubral system. This would indicate no correlation between the behavior of these animals and the behavior of decerebellate animals so far as the particular reactions in question are concerned. One must not overlook the temperamental factors, however, or the natural tendency of cats to resist manipulative procedures.

2. Another reaction of this series is that which demonstrates the influence of the position of the forelimbs on the *Stütz* tonus of the hindlimbs. Thus, when an intact, decorticate or decerebellate dog is placed with the forefeet on a firm supporting surface, the hindfeet resting on the palm of the observer's hand, and the trunk is moved caudalward so that the forelimbs slant forward from the shoulder, the hindlimbs extend toward the rear and offer considerable resistance to pressure against the soles of the feet. When the trunk is moved forward, the hindfeet also move forward; the *Stütz* tonus and resistance to pressure on the soles diminish, and the limbs tend to take flexed positions. Here again, temperamental peculiarities interfere with the successful execution of this reaction in the cat. In six of ten normal cats in our series the aforementioned procedure yielded negative results. In four, the effects were of variable intensity as regards the increase in *Stütz* tonus, and sometimes the reflex nature of the extension of the hindlimbs was questionable. Similarly, among cats with lesions in the red nuclei, considerable variation was found in the course of repeated examination. Three of seven cats undoubtedly gave positive responses. In each of the remainder the response was repeatedly negative, and only occasionally could one elicit a fair reaction. According to Rademaker, decerebellate animals give especially lively responses. One could hardly compare our cats with his animals on this basis, then.

3. The "to and fro" or *Schunkel* reaction is the third of the group, and involves the effect of the position of one limb on the *Stütz* tonus of the other. Here the influence of abduction or adduction of one limb is especially noticeable and may be demonstrated as follows: If one raises passively the right forefoot of a standing animal and then moves the trunk passively toward the right, causing abduction of the left, or standing, limb, there will be a strong abduction and extension of the raised forelimb. If the trunk is moved to the left, adducting the left limb, the right one is flexed and the *Stütz* tonus diminished. A more

detailed description of this reaction is omitted because of the excellent account given by Rademaker. It is to be inferred from Rademaker's remarks that in decerebellate animals the *Schunkel* reactions are somewhat delayed and prolonged; thus, adduction of the standing limb may cause the opposite one to be raised unusually high, and the ultimate extension caused by continued adduction of the standing limb is unduly retarded. In our experience, in normal cats the *Schunkel* reaction of the raised limb is of rather short duration and is soon broken into. For instance, if the raised limb is abducted and extended in response to abduction of the standing limb, this extension is not prolonged but is soon affected by flexion of itself or a sudden hopping adduction of the standing limb. After the raised limb has been extended a certain rather limited distance, these interrupting reactions occur. In general, under moderate abduction of the standing limb there is a noticeable increase of the *Stütz* tonus of the raised limb; under strong abduction, the tonus of the latter is ultimately decreased and there may be sudden flexor-extensor stepping reactions of one or both limbs, such as an animal may naturally make in maintaining its standing posture. In cats with lesions in the red nuclei, the *Schunkel* reactions are usually markedly prolonged, and the extension and abduction of the raised limb in response to abduction of the standing limb are well maintained, not being readily broken through by secondary movements of either limb. Continued strong, progressive abduction of the standing limb usually caused persistent abduction and extension of the raised limb. This was found to be the case in six of seven animals. One received the impression that as the postoperative period was prolonged there was some repression of the *Schunkel* reactions so that they more nearly approached the normal. The delay and overemphasis were characteristic of these cats, however, and there seem to be good grounds for comparing them with decerebellate animals. It may then be inferred that in this instance the derangement might be due to involvement of the efferent cerebellar pathway by the lesions in the red nuclei.

4. A fourth group of reactions demonstrates the effect of the position of a limb on its own *Stütz* tonus, and includes the so-called *Hinkebein* and *Stemmbein* reactions, which will be considered separately. As a result of careful study, it was concluded by Rademaker that the *Stütz* tonus of a standing limb is strongest when the latter is in the normal or so-called "middle position," in which it is usually almost perpendicular to the supporting surface and in such relation to the body of the animal that the weight of the body may be supported with least effort. Any deviation from this middle position, so that the limb slants one way or another, is said to cause changes in the *Stütz* tonus of the limb in question. Thus, when a foot which is under static tension is passively moved from the middle position a decrease in *Stütz* tonus

occurs, and the foot is raised and set down again nearer its optimum station. This raising and replacement of the foot has been called a *Hinkebein* (limping or hopping) step, and the whole reaction is called the *Hinkebeinreaktion*. It may be demonstrated by holding the animal in such a way that one foot only is resting, under tension, on the floor. The trunk is then moved passively one way or the other, causing the limb to be shifted automatically from the middle position and changing the angle of the shoulder. This causes a decrease in *Stütz* tonus and a *Hinkebein* step. Movement of the limb forward, medialward or toward the rear is effective in eliciting this reaction. In our experience with normal cats, the *Hinkebein* steps were found to occur promptly on moving the limb away from the middle position. The steps were rather short and quick, and did not involve an especially marked elevation of the foot. The reactions to forward and lateralward movement

Number of Hinkebein Steps for One Complete Rotation of the Turntable

	Medialward Movement of Limb	Backward Movement of Limb
Normal cats		
Forelimb	24.0	12.0
Hindlimb	20.0	10.0
Rubrectomized cats		
Forelimb	12.0	9.5
Hindlimb	11.5	8.8

of the trunk, which would, of course, mean backward or medialward movement of the limb, were found to occur with the most regularity, being least subject to voluntary or temperamental variations, and were chiefly used in this study. The *Hinkebein* reaction lends itself in some degree to measurement, and the length of the *Hinkebein* step may be estimated, furnishing an index of any delay or hypermetria. This has been done by Rademaker's method, the cat being held so that one limb rests on the edge of a turntable, which is rotated 360 degrees, the number of resulting *Hinkebein* steps being counted. The average number of *Hinkebein* steps for 360 degrees of rotation in six normal cats is shown in the table.

According to Rademaker, the *Hinkebein* reaction is lacking during the first days following the removal of the cerebellum. Later, however, it reappears but is never normal thereafter, as the *Hinkebein* step is delayed and occurs only after considerable change in the position of the limb. The step is also said to be hypermetric, the foot being lifted high and moved an extraordinary distance before it is set down again. Since the extent of each step is abnormally great, the number taken in traversing a certain distance is less than in the case of a normal animal;

thus, in using the turntable, the number of steps taken on rotation of the table 360 degrees is reduced by about one-half.

In most cats with lesions in the red nuclei, the *Hinkebein* reaction was found to be poorly executed or absent in the early stages following the operation. Later, it definitely appeared and was usually characterized by delay and excessive length of the steps. There was some variability, in part due to temperamental factors. The average number of *Hinkebein* steps taken on rotation of the turntable 360 degrees, based on repeated observations of eight cats with lesions in the red nuclei, is shown in the table.

Comparison of these figures for normal cats and for those operated on shows that the lesion caused a considerable hypermetria, especially as regards the steps resulting from medialward movement of the limbs. The responses to backward movement are but little more extensive than normal. There seems to be some justification, both from the standpoint of casual observation and from the results of measurement, for comparing the *Hinkebein* reactions of cats with lesions of the red nuclei with those of animals without the cerebellum.

Also to be considered in this group is the so-called *Stemmbein* reaction. This, which may well be termed the "bracing reaction," differs from the *Hinkebein* reaction in that movement of a standing limb toward the middle position causes the *Stütz* tonus of that limb to be increased. Thus, if an animal standing on all four feet is pushed or pulled gently toward one side, there will be a stiffening and bracing of the legs on the side toward which it is pushed. This reaction may also be demonstrated when the animal is placed on a board which can be tilted; as the board slants, the limbs on the lower side evidence an active bracing. Rademaker found this reaction to occur regularly in decerebellate animals, in which it seemed to be less subject to cortical inhibition than in normal ones. It was also exaggerated, so that unusually strong bracing was evident, especially to sideward and backward pull; this exaggeration was considered to be due in part to the wide base and backward extension of the limbs in decerebellate dogs.

In our experience we have found that while *Stemmbein* reactions are readily obtainable in normal cats, the cats are subjected to some vagaries of behavior. Many show a tendency to crouch; others, after a brief period of bracing, attempt to escape or take *Hinkebein* steps, and the voluntary element is quite conspicuous in their behavior. Cats with lesions in the red nuclei show poor or ordinary reactions in the early stages following operation, at which time there may be weakness or ataxia. Later, however, the *Stemmbein* reactions improve as the condition of the animal improves, until very strong bracing may be elicited by pulling or tilting the cat in any direction. The reaction is

more readily obtained in cats with lesions in the red nuclei than in normal cats, and seems to be less under the influence of the cortex. There may be some ground, then, for comparison of these animals with decerebellate animals. It is evident, however, that the reaction is not so strong in cats with lesions in the red nuclei as it is said to be in decerebellate cats, probably because the former do not take such an extraordinarily wide base of the limbs or show such strong *Stütz* tonus when standing as do decerebellate animals.

To sum up at this point, it is evident that cats with bilateral destruction of the red nuclei show certain characteristics of behavior which are similar to those which have been described as occurring in decerebellate animals. These characteristics are found in the increased response to *Stütz* stimulation when the animal is in the supine as well as in the upright suspended position, in disturbances of gait and in abnormalities of several postural reactions such as the *Schunkel, Hinkebein* and *Stemmbein* reactions.

Results of Incomplete Destruction of Red Nuclei.—As regards cats with incomplete involvement of the red nuclei, these animals show symptoms similar to those occurring after complete destruction of the nuclei, but to a degree more or less proportionate to the amount of damage to the rubral system. If one red nucleus is completely destroyed or more severely injured than the other, then the limbs on the side opposite to that nucleus show the most pronounced abnormalities, especially in regard to gait and tonus reactions. Cats with lesions of this type may also show some changes in the postural reactions, but here it is more difficult to distinguish differences in the limbs on the two sides of the body. Usually the ability to orient the head and trunk was retained, although this was sometimes interfered with by the onset of forced movements. As an example, one cat (38), which had practically complete destruction of the left red nucleus but only partial involvement of the right, showed intact labyrinthine and body righting reactions. Abnormalities of gait were most evident in the right limbs, which were observed to be excessively adducted. Fairly good *Stütz* reactions, which were strongest on the right, could be elicited. The *Hinkebein* reaction of the right limbs was late in appearing, but after recovery the postural reactions showed some exaggeration. Bilateral labyrinthectomy in these cats was found to produce the typical picture of labyrinthine deficiency; such an operation does not appreciably affect the *Stütz* and tonus reactions, but may accentuate any forced movement due to the lesions in the brain stem.

CONDENSED SUMMARIES OF THREE EXPERIMENTS

CAT 35.—From the time of the operation, Sept. 26, 1932, this cat was able to right itself and to walk, showing the usual gait, with ataxia, dysmetria and circumduction of the hindlimbs. There was little forced movement. The *Stütz* and

tonus reactions were at first pronounced when the cat was supine or in the suspended position, and the emphasis was decidedly on extensor tonus; these reactions diminished considerably as time went on, although on November 2 there were still fairly good *Stütz* reactions, especially evident in the left limbs. In December, this animal contracted enteritis, and it was killed on December 13.

Postural Reactions.—When first tested, about two weeks after operation, there were very good *Schunkel* and *Stemmbein* reactions; the *Hinkebein* reaction was exaggerated and delayed. Three weeks later the reactions were about the same, and four weeks later the extent of the *Hinkebein* steps on medialward movement of the limbs was found to be slightly less than double the normal average and increased about one third on backward movement.

Righting Reactions, Blindfolded.—The labyrinthine righting reactions were positive. The body-on-the-body righting reactions were positive, although somewhat delayed. The body-on-the-head reactions could not be tested.

Lesions.—The rostral poles of the red nuclei were damaged but not completely destroyed. Small areas of the compact portions in which there was great cellular degeneration remained, but the rubrospinal fibers were cut off by the lesions, and very few, if any, of the descending fibers could have escaped. Figure *A* illustrates the type of lesion in this instance.

Cat 36.—This cat, operated on on Sept. 28, 1932, was kept in good condition until Feb. 2, 1933, when bilateral labyrinthectomy was performed. From the first, the cat showed ability to right itself, to stand and to walk in the usual ataxic, dysmetric manner, with some evidence of temporary loss of position sense of the feet. In the early stages there was a tendency to circle to the right, which later disappeared. The gait and general coordination improved as time went on, but the effects of the lesions were retained in some degree until the last. The *Stütz* and tonus reactions were pronounced, and were still demonstrable at the end of the experiment.

Righting Reactions, Blindfolded.—The labyrinthine righting reaction to dropping and immersion was positive. The body righting reaction acting on the body was positive, but was somewhat delayed from the left side.

Postural Reactions.—Two weeks after operation the *Schunkel* reaction was marked and prolonged, the *Hinkebein* reaction was delayed and often exaggerated and the *Stemmbein* reaction was good. These reactions continued to be more pronounced than those of normal cats for the next month, and on November 8 the *Hinkebein* steps were found to be about double the normal extent on medialward movement of the limbs and to be considerably increased on backward movement. On December 28, quite similar results were obtained.

Following Bilateral Labyrinthectomy.—The body-on-the-body and visual righting reactions remained intact, and these were sufficient to orient the body, ventral side down. When the cat righted itself under compulsion, the pelvis was righted first, the rest of the body following. There was rather less excursion of the head than is usual in such animals, but in attempting to walk the cat showed considerable disorientation, with threshing of the limbs. The old tendency to curve to the right and fall to the left was reemphasized. The *Stütz* and tonus reactions were apparently not significantly changed. Death prevented further analysis of righting and postural reactions.

Lesions.—Owing to the lapse of from twelve to fourteen hours between the death of the animal and recovery of the brain, there was considerable postmortem change (the carcass was kept in the icebox overnight). However, the fibers and

cells stained fairly well, and there could be no doubt but that the red nuclei were completely destroyed throughout. The lesions were rather symmetrical and extended from the point where the habenulopeduncular tracts reach the ventral surface of the brain caudally into the decussation of the brachium conjunctivum. The oculomotor nerves were destroyed.

CAT 39.—This cat, operated on on Oct. 24, 1932, was kept under the influence of pentobarbital sodium for three days following the operation because of the tendency of rubrectomized cats to injure themselves during the first few days after the operation. On the fourth day this was discontinued, and the animal displayed ability to right itself and stand. Its movements were ataxic; *Stütz* and tonus reactions were marked, and there were some signs of excess sympathetic activity (erection of hairs). No forced movement was apparent. The gait during the earlier period showed overstepping and scissoring of the forelimbs, especially the left one, circumduction and some loss of position sense of the hindlimbs, with backward extension of the latter. These features persisted in marked fashion for a long time, as did the evidences of increased *Stütz* reactions, even as late as Feb. 6, 1933.

Righting Reactions, Blindfolded.—The labyrinthine righting reaction to dropping was positive. The body-on-the-body righting reaction was apparently positive, although struggling made the tests difficult.

Postural Reactions.—Four days after operation the *Schunkel* reaction was good, the *Stemmbein* reaction fair and the *Hinkebein* reaction variable and inconsistent. After one week the *Schunkel* reaction was better than average, the *Stemmbein* reaction fair, and there was evidence of exaggeration of the *Hinkebein* steps. On November 8, much the same was true, the left limbs showing hypermetria in the *Hinkebein* step; the extent of the steps on medialward movement of the limbs was considerably increased, while that on backward movement was normal. On December 28, the *Schunkel* reaction was normal, and the *Stemmbein* reaction somewhat exaggerated, while the extent of the lateral *Hinkebein* steps was double the average and that of the forward ones gave some signs of increase. Hypermetria was again in evidence.

Bilateral Labyrinthectomy.—This operation was performed on February 6; the cat, although it lay flat on the floor, persisted in orienting itself, ventral side down. When locomotion was attempted, it immediately became disoriented, showing excursions of the head, threshing movements and general agitation. Once, when excited, an ocular nystagmus with a quick component to the right was seen; this was not observed later. The *Stütz* and tonus reactions examined when the animal was supine showed hardly a significant change, perhaps being slightly enhanced. In general, the behavior remained typical of labyrinthless animals. After about a week there was some evidence of compensation; the cat was able to make progress in an uncertain manner and to return to its cage of its own accord. Some hypermetria was evident in the gait. Ten days after the operation, the *Schunkel* reaction was poor on account of refractory behavior of the animal; the *Stemmbein* reaction was good to pulling and also to tilting, if the latter was done slowly. The *Hinkebein* steps were somewhat less extensive than they had been on December 28. The labyrinthine righting reactions were, of course, absent, but the body righting reaction acting on the head was positive. The body-on-the-body righting reaction was also positive but somewhat delayed, especially from the left side.

Lesions.—The lesions extended from a level just caudal to the point where the habenulopeduncular tracts reach the ventral surface of the brain back to the

decussation of the brachium conjunctivum. They were slightly displaced to the right. The red nuclei were almost completely destroyed and all their connections apparently interrupted. A few scattered red nucleus cells remained on the right side, but it was difficult to see how any crossed connections could have persisted. Both interstitial nuclei were severely damaged, especially the left one, and the left nucleus of Darkshevich was atrophic, probably as a result of destruction of the left medial longitudinal fasciculus. There was somewhat extensive damage to the tegmentum on the right side, and some to the central gray matter on the left, with slight distortion of the aqueduct due to a needle puncture. Figure *B* illustrates the lesions.

Cat 43.—Following the operation, performed on Nov. 1, 1932, there were great ataxia and considerable weakness. The cat could apparently bring the body to an unright position. There was a slight concavity of the spine to the right. The *Stütz* and tonus reactions were fairly good. After several days it was able to move about readily and to right itself with ease. The gait was characteristic. There was a slight tendency to circle to the right. The *Stütz* and tonus reactions continued to be good and were strongest in the left limbs. By December 28, some recovery had supervened, but the gait and *Stütz* reactions remained characteristic. On Feb. 9, 1933, the cat showed a typical "nautical" gait, with overstepping of the forelimbs, especially of the left one, rotation of the pelvis and circumduction of the hindlimbs. There were at this time fair *Stütz* and tonus reactions, which were somewhat variable.

Righting Reactions, Blindfolded.—The labyrinthine righting reaction was positive. The body-on-the-body righting reaction was also positive from either side.

Postural Reactions.—Immediately following the operation the *Schunkel* reaction was marked; the *Stemmbein* reaction was present but not marked, and the *Hinkebein* reaction was absent. After five days the *Schunkel* reaction was good, especially in the left limbs; the *Stemmbein* reaction was fair, and the *Hinkebein* reaction was poor. Two days later, however, the *Schunkel* and *Stemmbein* reactions were good, and the *Hinkebein* steps lateralward showed a doubled extent, the forward steps also being increased about one-fourth. On December 28, the *Schunkel* and *Stemmbein* reactions were better than average, the lateral *Hinkebein* steps were double the normal extent, and the forward ones were somewhat increased in the hindlimbs. There was some indication of hypermetria.

Bilateral Labyrinthectomy.—On Feb. 9, 1933, bilateral labyrinthectomy was performed. Following this the behavior was typical. The animal lay flat on the floor, ventral side down. There were considerable excursion of the head and threshing of the limbs when the animal was thrown off balance, and a slight tendency to fall to the left, probably a consequence of the original forced movement. The cat became a victim of an epidemic of pneumonia before further study could be made.

Lesions.—The lesions extended rather far rostrad, and some damage was evident at the level of the caudal pole of the mamillary bodies, affecting chiefly the H_1 fields of Forel. Caudally, they extended into the decussation of the brachium conjunctivum. The right red nucleus was completely destroyed, but a few cells of the left remained, and there was a possibility that a few fibers from the left red nucleus may have escaped. The right nucleus of Darkshevich was slightly injured. Both interstitial nuclei were damaged, especially the right one. The lesions also affected the central tegmental fasciculi.

COMMENT

The observation that cats with the red nuclei destroyed may retain their ability to right themselves, stand and walk is in agreement with the work of other investigators. Pike, Elsberg, McCulloch and Chappell [5] found that certain animals are able to rise and walk within a few hours after median longitudinal section of the decussation of Forel, and that while others are temporarily incapacitated as the result of such an operation, in the course of time they are able to get about again in an efficient manner. Occasional forced movements, spasticity of the limbs and persistent hypermetria were also observed. It was concluded that lesions of the rubrospinal system may not necessarily abolish the righting reactions when the other motor systems remain intact. Ferraro and Barrera [6] described a cat in which a longitudinal section of Forel's decussation caused similar symptoms, and more recently Keller and Hare [7] denied that the rubrospinal system participated functionally in the righting and locomotor reactions. Further evidence is herewith adduced in support of that previously presented, together with the results of more careful and detailed analysis of the various righting reactions, all of which adds to the certainty that the red nuclei are only indirect participants or auxiliaries in the carrying out of these functions.

It is of some interest that several animals in our series hitherto not mentioned did display marked disorientation, inability to walk and partial loss of the righting reactions. There were three of these cats in our whole group of twenty-three animals. One of them, cat 98, showed rather typical behavior immediately following the operation and was able to right itself and to walk in the usual fashion. Between the second and fourth days, however, the symptoms became greatly aggravated, and the cat displayed complete disorientation, inability to right itself or to walk and evidence of pain. Examination of sections of the brain stem showed that during this period of change a hemorrhage must have occurred which tremendously enlarged the lesion on the right and undoubtedly caused severe pressure effects and necrosis. The lesions were excessively extensive and thus seemed to account for the late symptoms, but were too large to be consistent with the early behavior. Cat 33 presents a somewhat similar instance. On the first day after

5. Pike, F. H.; Elsberg, C. A.; McCulloch, W. S., and Chappell, M. N.: Some Observations on Experimentally Produced Convulsions: II. The Type of Convulsion Elicitable After Lesions of the Rubro-Spinal System, with Some Incidental Findings, Am. J. Psychiat. **10**:567, 1931.

6. Ferraro, A., and Barrera, S. E.: Experimental Catalepsy, Utica, New York State Hospital Press, 1932.

7. Keller, A. D., and Hare, W. K.: The Independence of Righting Reflexes and of Normal Muscle Tone from the Rubro-Spinal Tracts, Proc. Am. Physiol. Soc. 1933, Am. J. Physiol. **105**:61 (July) 1933.

operation this animal was able to right the forequarters and showed only faint indications of forced movement. There were great ataxia and considerable weakness, and the *Stütz* and tonus reactions were poor. The next day, however, there was pronounced forced movement which so twisted the spine that the forelimbs were swung to the right and the hindlimbs to the left, and the cat was unable to right itself from the left side. The *Stütz* and tonus reactions were much more marked. If walking was attempted, the cat soon fell onto its left side. The survival time was four days. On microscopic examination of the brain stem the lesions were found to be surrounded by a large area of softening, which extended forward into the retromamillary area and the gray of the third ventricle and caused great damage to the tegmentum of the midbrain, especially on the right side, destroying many structures, including the medial longitudinal fasciculi and associated nuclei. The delayed onset of the severe symptoms probably coincided with the development of the softening, which was probably of vascular origin.

Cat 31 was one of those in which the labyrinths had been destroyed long before the operation on the red nucleus. Following operation, there was not a good recovery. Ability of the cat to right itself from the right side was lost. There was severe forced movement, so that the spinal column was curved concavely to the right. The *Stütz* and tonus reactions were strongly increased, and the limbs could support the weight of the body. However, the ability of the animal to balance itself when standing was lacking. The wounds failed to heal, infection developed and the animal was killed. The lesions were found to extend from the retromamillary area into the pons. They were somewhat asymmetrical, the right one being rather close to the midline. The rubral system was completely destroyed, but the lesions were complicated and extended by softening, and involved especially an overly large area of the left side of the tegmentum. Both medial longitudinal fasciculi were destroyed, and the damage to the tegmentum was as extensive as in the other cats which were rendered helpless by the lesions. Here again the extension of the lesions was probably due to vascular involvement occurring soon after operation.

These cases demonstrate the necessity for lesions which are of restricted extent in investigating the functions of various areas of the interior of the brain. When these instances are compared with those in which the lesions were satisfactory, one can see how easily unfortunate errors of observation and interpretation can be made. The evidence presented here shows clearly that the destruction of the red nuclei, while producing various motor as well as postural disorders and disturbances of muscle tonus, does not affect labyrinthine or body righting reflexes. However, if the lesions are overextensive, destroying suffi-

ciently large areas of the tegmentum, the ability of the animal to orient itself is impaired, and a state of complete helplessness may develop. The extent to which this may be due to the occurrence of severe forced movements cannot as yet be stated. Whether these phenomena depend on damage to distinct structures or systems or are contingent on the degree of damage to the tegmentum as a whole has not at present been ascertained.

The similarities of the animals of this series to the decerebellate animals described by Rademaker, as shown by the study of their gaits and certain postural reflexes, are to us striking. That the abnormalities displayed by our animals were not so profound is sufficiently evident, but the resemblance is nevertheless interesting. In our opinion a considerable portion of the syndrome herein described must be due to the involvement of the great efferent cerebellar path which passes via the red nuclei. That not all of this pathway was involved is evident when one considers that the brachium conjunctivum descendens was hardly affected, and that a fair portion of the conjunctival fibers passing rostralward into the thalamus may have escaped in many instances, and variation in the profundity of the symptoms may perhaps be thus accounted for. One can hardly ascribe all of the disorders to injury of this system, however. It must be remembered that the red nucleus is also a focal point for the gathering of cortical, subthalamic and striatal impulses, and that the lesions were placed so as to involve, possibly, other important structures. In any case, its importance as an accessory motor structure is not to be doubted, nor can one deny that it is an active component of a motor system which is so complex that its analysis has not yet been successfully completed and which has far-reaching activities that may not always be significantly affected by the removal of a single one of its members. The red nucleus is concerned in a way with the regulation of muscle tone, plays its small part as a coordinator, and exercises restraint on certain motor activities; in these respects it may be subordinate to other, higher regions. That it is not essential to labyrinthine and body righting reactions may be reaffirmed. The manner in which these are carried out must be the subject of other investigations.

SUMMARY

1. Bilateral destruction of the red nuclei by lesions limited in their extent causes characteristic disturbances of gait and mild increases in extensor and *Stütz* tonus.

2. Such lesions do not affect the labyrinthine or the body righting reactions.

3. Certain postural reactions are delayed and exaggerated as an effect of these lesions; among these are the *Schunkel, Hinkebein* and *Stemmbein* reactions.

4. The disorders of gait, the increases in *Stütz* tonus when the animal is supine and the disturbances of the aforementioned postural reactions resemble greatly the symptoms appearing after complete decerebellation as described by Rademaker, and there is a possibility that the chief effects of lesions in the red nuclei may be ascribed to involvement of the premier cerebellar-efferent pathway.

EPILEPSY

TREATMENT OF INSTITUTIONALIZED ADULT PATIENTS WITH A KETOGENIC DIET

J. NOTKIN, M.D.
POUGHKEEPSIE, N. Y.

The object of this communication is to report the results of treatment of institutionalized epileptic patients with the ketogenic diet. I shall refrain from participating in the controversy regarding the mechanism operating in this form of therapy. It seems to me that no conclusive evidence has yet been offered that the acidosis, the ketone bodies or the dehydrating effect of the diet is the responsible factor. While there is an abundance of reports in the literature concerning the treatment of epileptic children with the ketogenic diet, there is a paucity of communications in reference to this form of therapy in adults. It seems that more favorable results are obtained in the treatment of children. There are three comprehensive reports in the literature regarding the treatment of adults. Two were made by Barborka in 1928 and 1930, respectively, and one by Bastible in 1931.

THE LITERATURE

In his first report, Barborka[1] gave the results of the treatment of thirty-two adults with epilepsy. Originally the number of patients was forty-nine. However, seventeen patients were on the diet for only from two to four weeks. In seven cases the attacks were controlled; twelve other patients were definitely improved, and thirteen patients were not benefited by the diet. In his second communication, Barborka[2] reported results in a group of one hundred adults with epilepsy. He concluded the report with the following statement: "One hundred adult patients, not observed in institutions, who were suffering from idiopathic epilepsy, were treated with a ketogenic diet. In twelve cases the attacks were controlled, and in forty-four the patients were definitely improved; thus fifty-six patients were benefited by the diet. Forty-four were not benefited and the treatment was considered a failure, although a number of patients were not maintained in a state of ketosis."

Bastible[3] reported his results in 1931; his material comprised a group of twenty-nine women who were psychotic institutionalized patients. The duration

1. Barborka, C. J.: Ketogenic Diet Treatment of Epilepsy in Adults, J. A. M. A. **91**:73 (July 14) 1928.

2. Barborka, C. J.: Epilepsy in Adults: Results of Treatment by Ketogenic Diet in One Hundred Cases, Arch. Neurol. & Psychiat. **23**:904 (May) 1930.

3. Bastible, C.: The Ketogenic Treatment of Epilepsy, Irish J. M. Sc. **2**:506 (Sept.) 1931.

of the ketogenic regimen was six months. Two patients showed a complete cessation of attacks during the last three months of the diet; the other patients showed a general tendency to a reduction in the number of attacks while ketosis was maintained. Six patients of this group suffered an increase in the number of convulsions while under treatment. It is important to mention here that Bastible had been giving his patients acid potassium tartrate in addition to the diet and that he also restricted their water intake. He did this in order to increase the state of acidosis. In the light of such additional factors, a correct evaluation of the results is difficult.

MATERIAL AND METHOD

The material for the study consisted of fourteen female and six male patients taken from the wards for the treatment of epilepsy at the Manhattan State Hospital. Twelve of the female patients were receiving, prior to the institution of the ketogenic diet, anticonvulsive therapy consisting of a bromide preparation or a combination of bromide and phenobarbital, or phenobarbital alone. The other two had received no therapy for many months. All the male patients were treated with phenobarbital only. A week prior to the day when the diet was to be inaugurated, therapy with drugs was discontinued, and no sedative medication was given during the whole period of the ketogenic diet. Analysis of the urine for acetone was made daily from the fourth day of the dietetic regimen. The patients were weighed twice a week, but only the original and the final weights at the end of the diet will be given in this report. As the study progressed new problems presented themselves and interests arose with regard to the basal metabolic variations and the changes in the blood sugar and blood count under the influence of the diet. In view of the gradual enlargement of the scope of the investigation, basal metabolic studies were made prior to and repeatedly during the course of treatment in ten cases only; in nine cases repeated basal metabolic readings were made during the period of the dietetic regimen, while in one instance no readings were made. As the observations of the blood sugar and the blood count prior to and during the diet showed no departure from the normal, no actual figures will be given further in this report.

The ages of the female patients ranged from 25 to 43 years, and the ages of the male patients from 22 to 47 years (table). The patients were suffering from the cryptogenic type of convulsive states. Practically every patient showed some degree of mental deterioration, but all understood the purpose of the diet and most of them cooperated well. Occasionally a patient would obtain food surreptitiously and on such occasions the acetone reaction in the urine would disappear. One female patient of the group had been free from attacks for several months preceding the period of diet; she was included in this group with the aim of ascertaining the influence that the diet might have on her mental state, which consisted of a mixture of epileptic deterioration and catatonic negativism. The longest duration of the period of diet in a single case was 729 days, the shortest, 108 days. Five patients received the diet from 108 to 200 days, twelve from 263 to 398 days, and three other patients from 632 to 729 days. The average duration for the whole group was 341 days.

In only one instance was I able to obtain a 100 per cent positive frequency of acetone in the urine during the duration of the diet. In eleven patients the frequency of a positive acetone reaction ranged between 99.5 and 92.4 per cent, with a leaning toward the higher figures. In three cases the percentage of positive acetone reactions ranged from 84 to 89.7 and in four cases from 78.1 to 71.9; in

one case the frequency of positive reactions was 51.9 per cent. The average percentage of positive reactions during the duration of the diet for the whole group was 89.5.

In order to ascertain the effect of the diet I have compared the number of convulsions recorded during the period of the diet with the number of attacks during a period of equal length preceding the period of diet when the patients were receiving some form of antispasmodic therapy or no therapy at all. In cases 2 and 5 such a comparison was impossible, as in the first instance the patient's residence in the hospital prior to the institution of the diet was shorter than the duration of the period of the diet, and in the second the patient was removed from the service several times during the period preceding the diet. However, in each case a comparison was made between the average monthly number of convulsions recorded before the diet and the average monthly number recorded during the diet.

RESULTS

With the exception of two instances there was an increase in the number of convulsions during the period of the diet as compared with the number of convulsions during an equal preceding period. In one case (5) there was a slight drop in the average monthly number of seizures during the period of diet. A comparison of the total number of convulsions during an equal preceding period was impossible in this case, as has already been mentioned. In some instances the increase in the number of convulsions during the dietetic regimen amounted to over 1,100 per cent, as in case 10. In case 1 the number of attacks increased 500 per cent. In other cases the frequency of convulsions trebled or doubled. This increase of attacks is noted especially in the monthly comparison of the number of seizures.

Considering the great increase in the number of convulsions in some cases the question arises whether this increase is not due to the cessation of the therapy with a sedative drug. This is difficult to answer, as unfortunately adequate control material is lacking. However, eighteen patients of this group, when originally admitted, received no treatment for a month for purposes of subsequent study of the effects of bromide and phenobarbital; every patient so treated showed a definite decrease in the number of attacks under the sedative therapy. I have compared the average monthly number of attacks during the period of the diet with that during the initial period of observation without medication and have found that in no instance was there a lower number of attacks during the period of diet; in a few instances there was an increase. Moreover, if the increase in seizures had been due to stopping the sedative drug, the increase probably would have been immediate and early in the dietary period. This was not the case. Two patients were entirely untreated prior to the diet, as in case 8, that of a woman who had eight convulsions during one year as compared with twelve attacks during the year while on the diet. While this is an increase of 50 per

Comparative Record of Patients on Ketogenic Diet

Case	Sex	Age	Days of Diet	Days Showing Negative Acetone Reaction	Days Showing Positive Acetone Reaction, per Cent	Convulsions During Period of Diet	Convulsions Equal Preceding Period	Average Month: Convulsions During Period of Diet	Average Month: Convulsions Preceding Period of Diet	Weight Before Diet	Weight on Cessation of Diet	Basal Metabolic Rating Before Diet	Basal Metabolic Rating at End of Diet
1	F	36	729	161	78.0	205	43*	8-9	0-2	96	160	+ 8.0	—16.0
2	F	41	722	55	92.4	180	..†	5	2	142	187	+ 1.4	—17.0
3	F	33	632	11	98.3	136	16*	6	1	132	194	.....	.....
4	F	39	398	64	84.0	117	56‡	8-9	4	173	193	.....	.....
5	F	30	387	22	94.4	171	..	13	16‡	158	163	—10.0	—11.0
6	F	43	366	96	73.8	98	40‡	8	3-4	95	135	— 2.0	—34.0
7	F	39	366	38	89.7	68	30‡	5-6	2-3	98	154	+ 2.0	—26.0
8	F	33	365	3	99.2	12	8‖	1	0-1	118	143	—20.0	—43.0
9	M	47	318	0	100.0	159	63‡	14	6	130	147	.....	.....
10	M	22	314	5	98.5	615	53‡	60	5	137	148	.....	.....
11	M	27	307	7	97.8	97	25‡	9	2	127	145	.....	.....
12	M	23	300	8	97.4	678	325‡	67	32	120	151	.....	.....
13	M	33	293	2	99.4	140	43‡	14	4	165	169	.....	.....
14	F	30	288	6	98.0	82	20§	7-9	2	112	143	.....	.....
15	M	23	263	29	89.0	108	55‡	11	6	128	140	.....	.....
16	F	41	185	52	71.9	40	12§	6-7	2	91	102	+ 8.0	—15.0
17	F	39	182	1	99.5	36	18‡	6	3	115	135	+ 9.0	—45.0
18	F	25	182	40	78.1	0	0‖	0	0	100	140	—17.0	—13.0
19	F	26	117	1	99.2	46	21‡	11	5	95	102	.....	.....
20	F	43	108	52	51.9	35	7*	10	2	93	112	— 4.0	—23.0

* Treatment with bromide and phenobarbital.
† The patient's residence in the hospital prior to the diet was shorter than the duration of the diet.
‡ Treatment with phenobarbital.
‖ No therapy.
§ Treatment with bromide.

cent this case is a rather mild one from the standpoint of frequency of convulsions and should not perhaps be used for comparison. The other untreated patient (18) had no seizures for six months preceding the diet and continued to remain free from attacks during the equal period of the diet. This instance will perhaps indicate that the diet did not have a deleterious effect on the patient.

As I have already mentioned, sedative treatment was discontinued a week prior to the institution of the diet in all cases in which treatment had previously been given; it is significant that no change occurred during that week or during the following week when the patients began to receive the diet. Of course, one week can hardly be considered as of sufficient duration to gage the effects of cessation of the sedative therapy, especially if it is borne in mind that bromide is rather slowly eliminated from the organism. In addition, the special care given to these patients might have produced a transitory favorable psychologic effect, especially during the first week of the diet.

I must emphasize here that I have failed to notice any relationship between the occurrence of a convulsion or a number of convulsions and the acetone content of the urine. I have records of a constant daily positive acetone reaction with frequent convulsions during the same periods. I have also observed patients with an entire absence of attacks during periods when no traces of acetone could be detected. I must add that convulsions have been noticed to occur on days when the patient showed a strong positive acetone reaction with the same frequency as on days when the reaction was negative.

OBSERVATIONS

In all instances there was a decrease in the weight of the patients during the first few weeks of the regimen, at the time when the total number of calories was relatively low. With the gradual increase in the number of calories a progressive gain in weight was noted. In some instances the gain was so pronounced that it was deemed advisable after one year of diet with the maximum number of calories to reduce gradually the number of calories. The decrease of the amount of food intake did not cause a decrease in weight, which remained stationary and showed no decrease during the rest of the period of diet. As is seen from the table, the majority of the patients showed considerable gain in weight at the end of the diet, some having gained more than 60 pounds (27.2 Kg.) in one year. The male patients did not show an increase of weight in the same proportion as the female patients. It is important, however, to bear in mind that none of the male patients was on the diet longer than 320 days, while the majority of the women received the diet for one year or longer. In addition, the male patients had more physical exercise than the female patients.

Basal metabolic readings were made in the cases of only ten patients prior to the institution of the diet (table). During that period the ratings ranged from

plus 9, the highest, in case 17, to minus 20, the lowest, in case 8. At the end of the diet period there was a decrease in the basal metabolic ratings in a great majority of the cases. In some instances the drop was particularly great. In case 6, for instance, the rating was reduced from minus 2 to minus 34; in case 17 the reduction was from plus 9 to minus 45. The decrease in the rating was a rather gradual one, as evidenced by the repeated readings during the diet period. In nine other cases basal metabolic readings were made only during the period of the diet. Except in cases 3, 9, 14 and 15, there was a general tendency to a decrease in the basal metabolic ratings as the diet progressed. In the six male patients of this group the readings were somewhat higher and showed less fluctuation during the diet as compared with the readings for the female patients. For the latter, however, more frequent metabolic determinations were made. In only one patient were no basal metabolic readings made.

It may be of interest that the female patients showed a greater gain in weight and a steeper drop of the basal metabolic ratings as compared with the male patients, the latter showing in general a moderate gain of weight and a smaller drop in the basal metabolic reading.

Four patients of the group died during the treatment; the rest are still living. In case 3, a woman, aged 33, sustained a fracture of the left ankle on the six hundred and ninth day and died suddenly on the six hundred and thirty-second day of treatment. In case 4, a woman, aged 39, sustained a fracture of the right ankle on the three hundred and eighty-third day of the diet and died suddenly 16 days later without apparent cause. In case 14, a woman, aged 30, died during an excitement following a convulsion on the two hundred and eighty-ninth day of the dietary regimen. In case 19, a woman, aged 26, contracted lobar pneumonia on the hundred and seventeenth day and died 3 days later. It is of interest that these patients were relatively young and that in two instances death occurred suddenly several days after fracture of a limb, and in another instance during a period of excitement. Whether the diet had any relationship to these deaths I am not prepared to state at present. The possibility of fat embolism in the sudden deaths may be considered.

SUMMARY

Twenty institutionalized patients with cryptogenic epilepsy were treated with a ketogenic diet for a period of from 108 to 729 days. The average duration of the diet for the whole group was 341 days. The ages of the patients ranged from 22 to 47 years. Each patient showed some evidence of mental deterioration. The acetone reaction in the urine was positive in 89.5 per cent of the total number of tests for the whole group during the entire period of treatment.

With the exception of two cases, there was an increase in the number of convulsions during the period of the diet. No relationship could be established between the occurrence of a convulsion or frequency of convulsions and the acetone content in the urine.

There was a loss of weight during the first two weeks of treatment followed by a gradual and consistent gain during the rest of the dietary period.

In ten cases basal metabolic readings were made prior to the institution of the diet and at certain intervals during the diet. Eight patients of this group showed a decrease of the basal metabolic rate during the diet, sometimes reaching very low values.

Patients with mental deterioration may respond to the ketogenic diet in a manner quite different from that of patients showing no mental deterioration.

NEUROLOGIC COMPLICATIONS OF EPIDEMIC PAROTITIS

REPORT OF A CASE OF PAROTITIC MYELITIS

CARLE B. McKAIG, M.D.
PINE ISLAND, MINN.
AND
HENRY W. WOLTMAN, M.D.
ROCHESTER, MINN.

It is said that no organ in the body escapes involvement in association with epidemic parotitis, yet complications are comparatively infrequent in the average epidemic. When the nervous system becomes involved, the alarming symptoms attract attention. It is estimated that about two hundred and fifty contributions dealing with involvement of the nervous system in cases of epidemic parotitis are listed in the *Index Catalog of the Library of the Surgeon General's Office* and in the *Quarterly Cumulative Index Medicus.*

MYELITIS

The following case of parotitic myelitis is reported, because of the rarity of the condition, and because it sheds some light on the nature of the neurologic lesions occasionally encountered. The subject is of sufficient practical importance to warrant general review.

In February, 1932, during a mild epidemic of mumps, a somewhat undernourished high school girl, aged 16, contracted the illness. At the end of twelve days she had apparently recovered. On March 1 she felt very well; she helped with the work around the house singing and cheerful and in exceptionally good spirits. On March 2 she complained of malaise, and was weak and tired during the day, and in the evening she complained of intense pain between the shoulder blades. The temperature and pulse were normal. On the following morning the pain was about the same, but during the day weakness of the legs developed, so that she had to be helped to the toilet. She was unable to urinate and had to be catheterized. After catheterization, she sat up, crossed her legs and talked spontaneously. The reflexes seemed to be normal at that time. On the morning of March 4, she complained of feeling as though she had been "novocained." The temperature was 99.2 F. There were almost complete inability to close the hands, marked weakness of the triceps muscles and complete flaccid paralysis of all of the muscles of the trunk and lower extremities. All superficial and tendon reflexes were absent. The anal sphincter was relaxed. The bladder was overfilled, but when the catheter was introduced suprapubic pressure had to be made to expel the urine. Anesthesia for all forms of sensation was complete below the second intercostal space and inner aspect of the arms. The neck was held rigidly. The optic

From the Section on Neurology, Mayo Clinic.

disks were slightly congested, but there was no edema. The spinal fluid was colorless and clear, and the pressure was 8 cm.; the compression test of the jugular veins was followed by a slow rise and fall of the fluid in the manometer. Kolmer's test was negative; Nonne's test was positive; 3 small lymphocytes and 1 neutrophil were present. The total protein was 200 mg. for each 100 cc. and the colloidal gold curve was 0011235210.

The findings indicated transverse myelitis at the level of the sixth cervical segment. Cultures were taken from Steno's duct and the nasopharynx; Rosenow injected these into rabbits. The rabbit inoculated with material taken from Steno's duct became paralyzed within one hour; the one inoculated with cultures taken from the nasopharynx became paralyzed within eight hours. Rosenow thought that there might be some association between this neurotropic organism and anterior poliomyelitis, and at his suggestion his antipoliomyelitis serum was administered to the patient. There was no improvement, but severe serum sickness developed. On the first day of the sickness the cutaneous reaction was general; subsequently it became localized to the hyperesthetic zone immediately above the line of anesthesia, where it was extraordinarily pronounced and was the site of intense itching. The sickness lasted about seven days.

Examination of the spinal fluid on March 21 revealed the presence of 7 lymphocytes and 2 neutrophils in each cubic millimeter; the protein content was 80 mg. in each 100 cc. and Nonne's test was positive. The patient was examined again on September 26. The right hand was bandaged to keep off drafts because of hyperalgesia and pain along the ulnar aspect; there was partial ankylosis of the fingers and wrists. Below the distribution of the second thoracic segment there were complete, flaccid, atrophic paralysis, as though all subservient cells of the anterior horns had been destroyed, areflexia and complete anesthesia. A jaw jerk was readily elicited, and the tendon reflexes of the arms were active. The sphincters were paralyzed and atonic. There was a decubital ulcer on the left foot. The neurologic picture was suggestive of extensive destruction of the spinal cord below the level indicated rather than of only transverse myelitis.

By Sept. 6, 1933, the patient's condition had not improved, and pyelitis had developed. Mentally, she was clear and bright.

CASES IN THE LITERATURE

The only other case of a similar nature that we have been able to discover was reported by Warrington.[1]

The patient was a girl, aged 17, who, with her brother, had bilateral parotitis about ten days previous to the examination. This condition was diagnosed, no doubt correctly, as mumps. On Friday she complained of pain at the back of the neck. On Sunday the pains were worse; on Monday the legs were weak and numb, and on Tuesday night the temperature rose to 101 F. She was slightly delirious. There was nystagmus in all directions. Flaccid paraplegia was complete, and reflexes were absent. The sphincter ani reflex was absent. The bladder was distended and urine dribbled. The thorax was paralyzed. There was total anesthesia on the right side up to the fifth dorsal segment and on the left as far as the first lumbar segment. Above this, sensation was diminished to the level of the second dorsal segment, which could be traced along the inner border of the

1. Warrington, W. B.: Acute Generalized Infective Paralyses in Adults, Clin. J. **43**:296 (May 13) 1914.

upper extremities. There was obviously involvement of the spinal cord up to but not involving the fifth or sixth cervical segment. The upper extremities were extensively paralyzed, especially the fingers and small muscles of the hands. The muscles supplied by the fifth and sixth roots acted fairly well. A week later the patient was obviously much worse. The anesthesia had become almost absolute. The action of the diaphragm was feeble. Death occurred two days later. Necropsy was not performed.

Missimilly [2] reported the case of a child, aged 5 years, who, a few days after an attack of mumps, suffered from flaccid paraplegia, and residual atrophy remained in the left thigh. The condition was referred to as poliomyelitis of mumps.

Bedingfield [3] reported a case of mumps and encephalitis in a boy, aged 9, in which the incontinence and the sloughing around the site of the spinal puncture suggested possible involvement of the cord; however, the patient was so desperately ill that the inference that myelitis was present is subject to question. He recovered within five weeks.

Sulzer [4] encountered a fatal case of epidemic parotitis, accompanied by a condition which he identified as multiple neuritis. However, necropsy was not performed, and Sulzer stated that myelitis could not be excluded with certainty. The patient was a woman, aged 37, who had incontinence associated with quadriplegia, absence of all tendon reflexes and bilateral diaphragmatic paralysis. Sensation, as tested objectively, was normal.

FACTORS OF AGE AND TIME OF ONSET

A person of any age may contract epidemic parotitis; the youngest patient in the series was aged 24 hours and the oldest was 99½ years. Contacts, such as occur in schools and military barracks, determine the age at occurrence to a large extent.

Neurologic complications usually occur in the course of the parotid swelling, as it is subsiding, or shortly thereafter, that is, from the third to the fourteenth day after subsidence. Intervals of three weeks and longer following the attack of mumps have been noted. Involvement of the nervous system may, however, precede the mumps. Taillens [5] found that in 19 cases, meningitis appeared before the parotitis in 5, with it in 4 and after it in 10. Indeed, it can no longer be questioned that neurologic disturbances may occur without any apparent parotitis and

2. Missimilly, quoted by Feiling, Anthony: Mumps: A Critical Review, Quart. J. Med. **8**:255 (April) 1915.

3. Bedingfield, Harry: A Case of Mumps Encephalitis, Lancet **1**:543 (March 12) 1927.

4. Sulzer, M.: Polyneuritis nach Mumps mit letalem Ausgang, Nervenarzt **1**:547 (Sept. 15) 1928.

5. Taillens, J.: La méningite ourlienne, Rev. méd. de la Suisse Rom. **48**:420 (April) 1928.

without orchitis, as evidenced by their appearance among siblings who have frank mumps, and in military barracks during epidemics of mumps. Abortive cases of parotitis are common and may not be recognized. Also, the incidence of neurologic complications varies with different epidemics. In Mayrhofer-Grünbühel's [6] experience with an epidemic, the first cases were mild; later cases were associated more and more frequently with orchitis, and finally there were several cases in which encephalitis was present. Brooks [7] found no evidence of meningitis in 1,059 cases of mumps at Camp Upton. Other observers have reported incidences of 1, 9, 25 and 100 per cent. Males are said to be affected three times more often than females.

Cases of epidemic parotitis that presented psychiatric and neurologic complications will be considered in the following sections.

PSYCHIATRIC DISORDERS

As a rule, psychiatric disorders are not common. Mumps, particularly when complicated by orchitis, may produce a violent systemic reaction; the most common psychiatric disturbance is delirium of a few days' duration.

Mitchell [8] reported the case of a Negro, aged 33, who, during an attack of epidemic parotitis, bit, fought, spat, and had to be restrained by three powerful men when an undescended testis became the seat of intense pain. The axillary temperature was 104 F. and the delirium lasted for four days.

Phillips [9] reported the case of a man, aged 23, who exhibited two periods of delirium, the first when the left testis became involved and the second, five days later, when the right testis became involved.

Hallucinations may be part of the picture. The psychosis is frequently described as mania, which may not subside entirely for several months. Depressive reactions have also been described. Van Bibber [10] reported the case of a man, aged 26, who had had parotitis, then orchitis. The patient had an idea that he could not get well and that he could not eat; the psychosis lasted for five months. Unfortunately, van Bibber's description is very brief.

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6. Mayrhofer-Grünbühel, Johanna: Enzephalitis nach Parotitis epidemica, Wien. klin. Wchnschr. **37**:1165 (Nov. 6) 1924.

7. Brooks, Harlow, quoted by Paddock.[15]

8. Mitchell, W. S.: A Case of Acute Orchitis Occurring in an Undescended Testis After an Attack of Epidemic Parotitis and Associated with Acute Delirium, Lancet **1**:23 (Jan. 7) 1911.

9. Phillips, Sidney: Note on a Case of Mumps in Which Attacks of Epididymitis Occurred on Each Side in Turn, Each Attack Being Accompanied by Symptoms Profoundly Involving the Nervous System, Lancet **1**:23 (Jan. 7) 1911.

10. Van Bibber, John: Three Cases of Metastatic Insanity Following Parotitis, M. News **47**:678 (Dec. 19) 1885.

Another case was that of a young medical student who, following an attack of orchitis and parotitis, became depressed and suicidal and thought himself guilty of imaginary crimes.[11] The duration of the psychosis was not reported.

Gentry's patient,[12] a boy, aged 8, recovered from ataxic, dystonic and choreiform movements, but for months exhibited a behavior disorder in all respects like that occasionally observed with epidemic encephalitis.

MENINGITIS

The first case of meningitis is said to have been described by Hamilton in 1758. A probable case of parotitic meningitis was described in 1850 by Minot.[13] His report of a case of cynanche parotidaea with metastasis to the testis and cerebral complications is of interest:

> Mr. A., a gentleman of about 50, tall, thin, with dark complexion, hair and eyes, of strongly marked nervous temperament, habitually dyspeptic and low spirited, frequently complaining of pain in the head, was more unwell than usual on the ninth of August, 1849. . . . The hands were constantly applied, one to the head, the other to the scrotum, supporting the testicle. After seven days of treatment with infusion of senna and manna, sinapisms, evaporating lotions to the head, calomel, colocynth, bleeding, twenty leeches to the temples, croton oil to the head, which he rubbed into his eyes, and many consultations, the pain was better, the mind pretty clear, though weak; he burst into tears on seeing his friends.

Laboratory methods of examining the spinal fluid have placed the diagnosis of parotitic meningitis on a firm basis. In most cases the meningitis, with its customary symptoms and signs, appears within the first two weeks of the parotitis. It may remain asymptomatic, detectable only on examination of the spinal fluid, or it may appear foudroyant. Thus, Colomb and Mercier [14] reported the case of an army officer who was found in the barracks in a comatose state, with dilated pupils, a rigid neck and positive Kernig's sign; three days later, evidence of parotitis appeared. Convulsions also may occur in such cases, and early deaths have been reported. It is probable that encephalitis was present in these cases. A report of mumps associated with meningitis in identical twins was contributed by Paddock.[15]

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11. Smith, R. P.: Insanity Following Mumps, Lancet **2**:265 (Aug. 10) 1889.

12. Gentry, W. J.: Mumps with a Double Complication of Meningitis and Pancreatitis, Nebraska M. J. **17**:383 (Sept.) 1932.

13. Minot, Francis: Case of Cynanche Parotidaea with Metastasis to the Testicle and Cerebral Complication: Convalescence in Ten Days, Am. J. M. Sc. **20**:377, 1850.

14. Colomb and Mercier, quoted by Weissenbach, Basch and Basch.[18]

15. Paddock, B. W.: Mumps Associated with Meningitis in Identical Twins, Am. J. Dis. Child. **44**:565 (Sept.) 1932.

The course of the meningitis is usually benign. Repeated spinal punctures and drainage for the purpose of lowering the tension of the fluid to normal levels are clearly indicated. Wallgren [16] suggested that the cause of acute aseptic benign meningitis is to be found associated with mumps rather than with poliomyelitis or encephalitis, even when parotitis is not present. The slow pulse so frequently observed with mumps has been attributed to vagotonia, but just what brings this about is not explained. Undoubtedly increased intracranial pressure is often present in these cases.

ENCEPHALITIS

Encephalitis is probably the gravest complication of epidemic parotitis. Eberle [17] reported the case of a patient who had convulsions and died within an hour. On the whole, however, fatalities from encephalitis are not common. In some cases residual complications persist for months, but usually clear up eventually; recovery from apparently severe complications appears to be the rule and often occurs within two weeks. The symptoms apparently often have a vascular basis, since hemiplegia and hemianesthesia are among the commoner occurrences mentioned. Extension into the cortex from the meninges is known to occur. It is not surprising, therefore, that the list of disabilities is a varied one and in some cases indicates multiple foci: hemiplegia, with or without aphasia; hemianesthesia, with or without aphasia; paralysis of one arm and the opposite leg; emissive or receptive aphasia; agraphia; conjugate deviation of the eyes; ataxia, presumably due to cerebellar involvement; trismus (cause?); chorea; myoclonia; herpes, and combinations of these with palsy of the cranial nerves, especially the seventh nerve. The following is a typical case: [18]

A man, aged 28, was driving his car to work when his vision suddenly became blurred and he saw double. The right side of the body felt like wood, and his head began to ache. He attempted to telephone to his fiancée but was unable to understand what she said and had some difficulty in expressing himself. Neurologic examination gave negative results; the patient refused to permit a spinal puncture. Three days later, he felt well but had mumps.

The sequence of events in some cases remains doubtful, as in the one reported by Haldeman.[19]

A man, aged 21, had both parotitis and orchitis. On the sixth day, syncopal attacks appeared and right hemiparesis developed; three days later the left side

16. Wallgren, Arvid: Méningite ourlienne sans oreillons, Acta pædiat. **6**:53, 1926.

17. Eberle, quoted by Minot.[13]

18. Weissenbach, R. J.; Basch, Georges, and Basch, Marianne: La méningite et la méningo-encéphalite ourliennes primitives, Ann. de méd. **27**:5 (Jan.) 1930.

19. Haldeman, F. D.: Unusual Metastasis in Mumps: With Report of Three Fatal Cases, J. A. M. A. **8**:543 (May 14) 1887.

became paralyzed. On the sixth day after the onset of neurologic symptoms, the patient coughed; there was a gush of pus from the throat and he died. Necropsy was not performed.

That the basal ganglia may be involved is indicated in a case reported by Bedingfield.[8]

A boy, aged 5, had been exposed to mumps two weeks before examination. Pain appeared suddenly in the legs; the temperature rose to 104 F.; the right knee became swollen; two days later he became semicomatose. On the sixth day of the illness signs of bronchopneumonia were discovered, and the patient became unconscious; the neck became retracted and the arms rigidly extended. The spinal fluid was clear, but lymphocytosis was severe. The tendon reflexes disappeared, and the Babinski sign was positive bilaterally. There was incontinence, and sloughing at the site of a spinal puncture. The right external rectus muscle became paralyzed. On the eighth day of the illness, the facies was masked, and a diagnosis of epidemic encephalitis was made. Anuria appeared and lasted for seventy-two hours. On the ninth day, myoclonus of the neck, thigh and abdominal muscles was revealed, and on the tenth day bilateral parotitis. The patient recovered completely.

Sicard [20] reported the case of an obese boy, aged 15, who at the age of 2 had parotitic meningitis, and several weeks thereafter progressive hydrocephalus, causing a condition resembling multiple sclerosis. In this case the cerebral signs were probably secondary to the hydrocephalus and the hydrocephalus secondary to the meningitis.

NEURITIS

Although the terms neuritis and polyneuritis appear frequently in the literature on parotitis, with the implication that the lesion is in the peripheral distribution of the affected nerves, it seems more likely that the conditions encountered are secondary to meningitis, so that the term meningoradiculitis would be more appropriate. Cases in which all four extremities were paralyzed have been described; the tendon reflexes were usually absent, subjective numbness may have been complained of, but superficial sensation as tested objectively was usually found unimpaired and tenderness was not striking. Some diminution in perception of vibration, of changes in position and of stereognosis was occasionally observed, and Babinski's sign was at times found to be positive; control of the sphincters was usually preserved.

Paralysis of some cranial nerves may be associated with flaccid tetraplegia, as in Revilliod's case,[21] that of a boy, aged 7, who recovered but who had paralysis of both abducens nerves, of the left facial nerve and of the right hypoglossal nerve; he required feeding by tube.

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20. Sicard, J. A.: Hydrocéphalie acquise par méningite ourlienne, Rev. neurol. **22**:706 (May 7) 1914.

21. Revilliod, L.: Paralysie ourlienne, Rev. méd. de la Suisse Rom. **16**:752 (Dec.) 1896.

A man, aged 23, had paralysis of both facial nerves in addition to the tetraplegia.[22] In the report of 3 cases of bilateral facial paralysis, Nemlikher,[23] Dopter [24a] and Sulzer [4] stated their belief that the virus extends directly from the parotid gland into the peripheral part of the nerve. In 1 case there were, besides paralysis of the left facial nerve,[23] paralysis of the palate and the right half of the tongue and paresis of accommodation.[24a] In a case of tetraplegia with lost reflexes the patient, a woman, aged 37, succumbed when bilateral diaphragmatic paralysis developed.[25]

A rare type of paralysis occurred in the case of a man, aged 22, who, twenty days following an attack of parotitis and orchitis, experienced pain in the right shoulder, arm and forearm, and ten days thereafter complete paralysis of the upper brachial plexus (Duchenne-Erb type). There was slight hypesthesia over the region of the deltoid muscle. The spinal fluid was normal.[24b]

In a similar case [26] the clinical picture was that of Aran-Duchenne's atrophy, the lesion corresponding to the eighth cervical and first thoracic segments. A soldier, aged 21, contracted mumps and orchitis and, one week after this, experienced weakness in the small muscles of the right hand, which fibrillated and atrophied. Horner's syndrome (cervical sympathetic paralysis) was noted on the same side. The spinal fluid contained 6 lymphocytes to each cubic millimeter, and the content of sugar was slightly increased. It was clear that the lesion involved the lower motor neurons, but whether it was in the anterior roots, a meningoradiculitis, or in the anterior horn cells, a subacute poliomyelitic process, was not decided; the authors favored the latter view.

Herpes involving the face or trunk associated with mumps has been described in several cases.[27] Butler [28] described the case of a girl, who,

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22. Collens, W. S., and Rabinowitz, M. A.: Mumps Polyneuritis, Quadriplegia, with Bilateral Facial Paralysis, Arch. Int. Med. **41**:61 (Jan.) 1928.

23. Nemlikher, L. J.; Chernikov, V. V., and Solomonowa, S. J.: Doppelseitige Facialislähmung bei Parotitiden die mit Symptomen infektiöser Polyradiculoneuritis verlaufen, Deutsche Ztschr. f. Nervenh. **125**:292 (April 14) 1932.

24. Dopter, C.: (*a*) Paralysie faciale ourlienne: Lymphocytose du liquide céphalo-rachidien, Bull. et mém. Soc. méd. d. hôp. de Paris **21**:912 (July 29) 1904; (*b*) La méningite ourlienne, Paris méd. **1**:35, 1911.

25. Thompson, W. R.: Thrombosis of the Sigmoid and Cavernous Sinuses Following Mumps, Texas M. Gaz. **4**:295 (Oct.) 1904.

26. Janbon, M.; Jarry, R., and Henriet, P.: Main d'Aran-Duchenne consécutive à une maladie ourlienne, Arch. Soc. d. sc. méd. et biol. de Montpellier **10**:261 (June) 1929.

27. Roger, H., and Margarot, J.: Le zona ourlien; à propos d'un cas de zona au cours d'une méningite ourlienne, Rev. de méd., Paris **29**:826, 1909. Sicard, J. A.: Un cas d'oreillons, avec zona du trijumeau et lymphocytose rachidienne, Bull. et mém. Soc. méd. d. hôp. de Paris **22**:135, 1903.

28. Butler, T. H.: Third Nerve Paralysis After Mumps and Chicken-Pox, Brit. M. J. **1**:1095 (June 14) 1930.

following an attack of mumps, had paralysis of the palate and of the pupils to light and in accommodation, a combination which usually follows diphtheria. That the auriculotemporal syndrome, reviewed by Bassoe,[29] may occur was shown in a case reported by Trioumphoff,[30] in which chewing produced local flushing of the face accompanied by a sensation of warmth and tingling, which was followed by sweating.

NEURO-OPHTHALMOLOGIC COMPLICATIONS

Of the nerves supplying the extra-ocular muscles, the sixth appears to be most susceptible. Presumably implication by way of the meninges is responsible. Fixed pupils and paralysis of accommodation have been reported occasionally. Loss of vision may involve one eye or both; it may be partial or complete, temporary or permanent. Woodward[31] reviewed the various lesions responsible. These include optic neuritis and neuroretinitis, retrobulbar neuritis and optic atrophy. He also reported the details of the examination of an enucleated eye. The patient was a girl, aged 11, who had parotitic neuroretinitis resulting in blindness, secondary glaucoma and staphyloma, with enucleation of the eyeball three and a half years later. Section of the optic nerve disclosed complete atrophy, replacement with hyalin and obliteration of the small vessels of the sheath of the nerve. A case in which bilateral choked disks had been observed was reported by Larkin.[32] The resultant changes in the fields of vision were of course noted by some of the observers.

COMPLICATIONS AFFECTING THE EIGHTH NERVE

Of the acute infectious diseases, it is said that mumps, next to scarlatina, most often affects hearing. Hubbard[33] has stated that from 3 to 5 per cent of deaf-mutism in the United States is due to mumps.

When deafness complicates mumps it is usually complete and permanent, but fortunately it is unilateral in about 75 per cent of cases. The affected ear may be on the side opposite that of the swollen gland. Sometimes there is neither parotid nor testicular swelling, yet circumstances indicate that the agent responsible for epidemic parotitis is responsible for these cases of deafness also. The onset of the deafness

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29. Bassoe, Peter: The Auriculo-Temporal Syndrome and Other Vasomotor Disturbances About the Head, M. Clin. North America **16**:405, 1932.

30. Trioumphoff, A.: Une forme particulière de l'hyperhidrose locale de la face, Presse méd. **2**:1350 (Oct. 27) 1926.

31. Woodward, J. H.: The Ocular Complications of Mumps, Ann. Ophth. **16**:7 (Jan.) 1907.

32. Larkin, W. R.: Mumps Meningitis Found at Camp Taylor Base Hospital with Autopsy Findings, Illinois M. J. **38**:133 (Aug.) 1920.

33. Hubbard, Thomas: Nerve Deafness and Mumps, Tr. Am. Otol. Soc. **13**: 451, 1915.

usually occurs within the first two weeks. It is usually rapid; some cases are reported in which the patients were completely deaf when they awakened in the morning.[34] Tinnitus occurs in about half of the cases, and in about half also there are vertigo and its usual concomitants, nausea, vomiting and nystagmus, indicating involvement of the vestibular portion of the nerve. Caloric reactions may be absent. Recovery from the vertigo is to be expected.

Just what takes place in these cases is not known, but the most reasonable and generally accepted explanation is that a sudden exudate into the labyrinth occurs. Hubbard has advocated spinal puncture as an aid in decompression. If the current explanation is correct, the injection of a hypertonic solution of dextrose may prove useful. Apparently the only examination of the pathologic process of the ear is that recorded by Toynbee,[35] who found complete disorganization of the nervous apparatus in the labyrinth and a dark fluid in the vestibule and cochlea.

THE SPINAL FLUID

The pressure of the fluid is usually increased when clinical evidences of meningitis exist, although manometric readings are rarely given. In some instances the fluid has been reported as slightly clouded, but it is almost always clear and colorless. A few cases have been reported in which there was no pleocytosis, but in most of them the cell count is high, sometimes reaching 3,000 in each cubic millimeter. In Gentry's [12] 2 cases about 75 per cent of the cells were of the neutrophilic type, and Holtz [36] reported a case in which polymorphonuclear leukocytes predominated; but on the whole the cells are of the lymphocytic type, and usually only lymphocytes are found. There can be no doubt that the spinal fluid is often altered, even when there is no clinical evidence of involvement of the nervous system. Thus, Monad [37] found pleocytosis in 6 of 8 cases in which puncture had been done. De Massary, Tockmann and Luce [38] asserted that in all cases of mumps, whether or not the nervous system is affected, pleocytosis may be present, but not necessarily at the time of the first puncture. This conclusion was reached

34. Burnett, S. M.: Absolute Loss of Hearing-Power in Both Ears Accompanying an Attack of Mumps, Arch. Otolaryng. **14**:19, 1885.

35. Toynbee, quoted by Mauthner, Oscar: Die Erkrankung des Nervus octavus bei Parotitis epidemica, Arch. f. Ohren-, Nasen- u. Kehlkoph. **87**:223 (May 15) 1912.

36. Holtz, Karl: Mumpsmeningitis, Deutsche med. Wchnschr. **57**:536 (March 27) 1931.

37. Monad, quoted by Feiling, Anthony: The Blood and the Cerebro-Spinal Fluid in Mumps, Lancet **2**:71 (July 12) 1913.

38. de Massary, M. E.; Tockman, M., and Luce, M.: Méningite lymphocytique et syndrômes nerveux dans les oreillons, Bull. et mém. Soc. méd. d. hôp. de Paris **41**:847 (July 6) 1917.

after repeated punctures were made on 56 patients with epidemic parotitis. The cell count returned to normal usually by about the fiftieth day. The authors believed that the presence of neutrophilic cells indicates secondary infection. They found some increase in albumin, diminution in chlorides and a slight increase in dextrose. Their conclusions may be too sweeping; nevertheless, they observed pleocytosis sufficiently often so that it should be reckoned with whenever the nature of epidemic parotitis is being considered.

The other changes in the fluid are not constant. There may be an increase in the content of protein; the chlorides may be slightly decreased, the sugar changed, and the bacteriologic observations negative,[18] although the finding of streptococci has been reported by a few observers; the colloidal gold curve may indicate a meningitic reaction.

OBSERVATIONS OF THE PATHOLOGIC PROCESSES

Although there are many references in the literature dealing with the clinical aspects of the cerebral complications of mumps, the references to studies of the pathologic processes are few. The low mortality rate, from 0.012 per cent, in Denmark, to 0.15 per cent, in the United States during the Civil War period, explains this in part.[39]

Maximovitch [40] described the surface of the brain as being edematous, the sulci as being filled with a semifibrinous exudate and the pons and cord as being hyperemic. Necropsy was performed on Dopter's [24b] patient, who died six hours after the appearance of meningeal symptoms. The convexity of the brain was almost normal, the pia was lightly injected, and an opalescent, almost transparent gelatinous edema surrounded the cranial nerves. Microscopic sections were not made.

Acker [41] reported the case of a boy, aged 3 years, who died after an illness of eighteen days, during which he had had generalized convulsions, right hemiplegia, fixed pupils and strabismus. Necropsy disclosed marked venous congestion of the vessels over the vertex and evidence of meningitis with fibrinous plaques over the base; on section the substance of the brain was found normal.

Unfortunately, Bien's [42] report of an obviously careful study of the pathologic process of the brain of a girl, aged 8, who had died in

39. Wesselhoeft, Conrad: Mumps: A Review of Our Knowledge Concerning Its Etiology, Mode of Transmission, Incubation and Period of Infectivity, Mil. Surgeon **46**:63 (Jan.) 1920.

40. Maximovitch, quoted by Casparis, H. R.: Cerebral Complications in Mumps, Am. J. Dis. Child. **18**:187 (Sept.) 1919.

41. Acker, G. M.: Parotitis Complicated with Meningitis, Am. J. Dis. Child. **6**:399 (Dec.) 1913.

42. Bien, Gertrud: Encephalitis bei Mumps, Verhandl. d. Versamml. d. Gesellsch. f. Kinderh. **30**:288 (Sept.) 1913.

convulsions on the ninth day after she had contracted mumps, is too brief. Slightly cloudy, thickened, moderately hyperemic and infiltrated meninges were found. Adventitial accumulations of fat-bearing cells were present. The striking finding was sharply demarcated insular defects in the medullary portion of the cortex. The relationship of these to the blood vessels is not stated. Nevertheless, this finding reminds us of the perivascular myelinoclasis reported by Marsden and Hurst [43] as occurring when encephalopathy is associated with smallpox, vaccinia and some of the other acute infectious diseases. They contended that the acute infections, regardless of their nature, precipitate a demyelinizing type of encephalitis of common etiology.

Necropsy reports by Gordon [44] in 4 cases are often referred to, but without discussion. The cases are carefully reported and therefore important, except that there may be some doubt as to whether the disease was epidemic parotitis or an unknown disease. The cases occurred during an epidemic of mumps. The patients were 3 boys and a girl, aged less than 10 years, who died on the first, second, third and twelfth days of the illness. All had some fever, a fast, weak pulse, vomiting and diarrhea; they became comatose and generally rigid. In 3 cases Kernig's sign was positive and the patellar reflexes were lost; in 2 cases there were convulsions; the pressure of the spinal fluid was increased, and there was pleocytosis, the predominant cells being lymphocytes. In only 1 case was the parotid gland somewhat enlarged clinically. In all of the 4 cases the salivary glands contained foci of acute interstitial inflammation; the meninges were congested and variably infiltrated with lymphocytes. There was some increase in glia cells and wasting and chromatolysis in some anterior horn cells. In only a single case was there intramedullary perivascular infiltration around a vessel near the floor of the fourth ventricle.

Voisin's [45] patient, a man, aged 34, was an alcoholic addict, who died after an illness of three days, during which there was conjugate deviation of the head and eyes toward the left, swelling of the parotid gland, meningeal irritation and cloudy sterile spinal fluid which contained chiefly polymorphonuclear leukocytes. He reported finding a yellow exudate over the vault and base of the brain and posterior surface of the cord. One is led to infer that only gross sections of the brain were made.

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43. Marsden, J. P., and Hurst, E. W.: Acute Perivascular Myelinoclasis ("Acute Disseminated Encephalomyelitis") in Smallpox, Brain **55**:181 (June) 1932.

44. Gordon, M. H.: On a Fatal Illness in Children Associated with Acute Interstitial Parotitis, Lancet **2**:275 (Aug. 2) 1913.

45. Voisin, Roger: Un cas mortel de méningite ourlienne, Bull. et mém. Soc. méd. d. hôp. de Paris **1**:223 (Feb. 18) 1916.

Larkin reported the case of a soldier, who died on the sixth (?) day after an illness during which enlargement of the parotid glands, delirium, a positive Kernig sign and choked disks developed. The spinal fluid was clear; it contained 200 cells, 40 per cent of which were of the polymorphonuclear type and 60 per cent of the lymphocytic type. Necropsy disclosed early bronchopneumonia, splenitis, nephritis, extensive accumulation of slightly turbid fluid in the cisterna magna, congestion of the pia-arachnoid and a greenish-yellow exudate along the blood vessels. The ventricles were somewhat dilated and the surfaces slightly granular; microscopically, the leptomeninges were densely infiltrated with large and small mononuclear cells. Perivascular infiltration extended into the cortex; cultures of the spinal fluid were sterile.

Fábián's [46] case was that of a child, aged 4 years, who one week after apparent recovery from parotitis had headache and a stiff neck, vomited and became unconscious; the spinal fluid was under increased pressure; globulin was increased and there were from 20 to 25 lymphocytes and from 4 to 5 leukocytes in each cubic millimeter. Death occurred on the seventeenth day. Necropsy disclosed tuberculous nodes at the hilus, bronchopneumonia, internal and external hydrocephalus and an infiltration with leukocytes and lymphocytes about the congested vessels of the meninges.

That mumps may be complicated by thrombosis of the sigmoid, inferior petrosal and cavernous sinuses was verified at operation by Thompson. A man, aged 52, contracted mumps with swelling of the left parotid gland. Nine days later marked protrusion of the left globe, chemosis and dilatation and fixation of the pupil developed. A clot was evacuated from the left sigmoid sinus. Six hours later similar changes appeared in the right eye, and the patient died. Necropsy was not performed.

All in all, then, there is pathologic evidence of meningitis associated with mumps. Intramedullary perivascular infiltration has been found, but it has always been slight and leaves one unsatisfied with the explanation of some of the clinical findings; I could find no reports of pathologic studies of the peripheral nerves and nerve roots. For convenience, the accompanying table gives the salient pathologic data of all reported cases so far as we could discover them.

EXPERIMENTAL STUDIES

Experimental methods to help solve clinical problems must be employed cautiously; the observation of processes more or less under control, however, always affords fruitful suggestions.

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46. Fábián, Ludwig: Beiträge zum Krankheitsbild der Meningitis parotidea, Monatschr. f. Kinderh. **38**:210, 1928.

Wollstein [47] observed that when she injected the filtered mouth washings from 4 children who had been ill for two or three days with mumps into the subarachnoid space of cats, a condition developed which was characterized by strabismus and increased pressure of the spinal fluid, which contained an excess of globulin and marked pleocytosis, with 84 per cent neutrophilic cells and 16 per cent mononuclear leukocytes. The cats recovered on the sixth day. Necropsy on another animal killed on the third day disclosed a cloudy, congested, edematous pia and some perivascular accumulation of leukocytes.

Summary of the Pathologic Data Reviewed

		Meninges		Brain			
Author	Year	Cloudy Exudate	Congested	Congested	Perivascular Infiltration	Myelinoclasis	Comment
Maximovitch	1880	+	..	+	..	..	Hyperemia of pons and cord
Dopter	1911	+	+	..	..	..	Died six hours after onset of meningitis
Acker	1913	+	+	0	0	0	Convulsions, strabismus, hemiplegia
Bien	1913	+	..	..	..	+	Convulsions
Gordon 1?	1913	+ Lymphocytosis	+	+	0	..	In all cases coma, muscular rigidity, increased glial cells, chromatolysis of the anterior horn cells
2?		+ Lymphocytosis	+	+	0	..	
3?		+ Lymphocytosis	+	+	0	..	Flattened convolutions, pressure cone
4?		++ Lymphocytosis	+	+	+*	..	Flattened convolutions, pressure cone
Voisin	1916	++	..	..	..	..	Conjugate deviation, meningeal signs
Larkin	1920	+++ Mononuclear	+	..	+	..	Delirium, meningeal signs, choked disks
Fábián	1928	++ Lymphocytosis and neutrophilia; perivascular infiltration	++	+?	..	+?	Meningeal signs, hydrocephalus, beginning necrosis (brain ?) in places
Thompson	1904	.....	..	..	..	..	Thrombosis of sigmoid, inferior petrosal (and cavernous) sinuses (operative case)

* One vessel fourth ventricle.

Gordon [48] inoculated 10 monkeys intracerebrally with washings passed through a Berkefeld filter. Four of the monkeys died with evidences of cerebral disorders. Degenerative changes were found in the nerve cells, and in one monkey cortical encephalitis, as evidenced by perivascular infiltration, was found.

A monkey (Macacus cynomalgus) that had been inoculated intracerebrally and intraperitoneally had on the fifth day 1,500 cells (82 per cent lymphocytes, 12 per cent polymorphonuclear leukocytes, 6 per cent

47. Wollstein, Martha: Experimental Mumps Meningitis, J. Exper. Med. **34:** 537 (Dec.) 1921.

48. Gordon, M. H.: Experimental Production of the Meningo-Encephalitis of Mumps, Lancet **1:**652 (March 26) 1927.

endothelial cells) in the spinal fluid; the monkey died on the ninth day. Cultures were sterile. The pia-arachnoid was infiltrated with lymphocytes; the spinal cord and cerebral cortex were hyperemic; vessels were occasionally ruptured and a considerable proportion of the nerve cells were markedly degenerated.

DIFFERENTIAL DIAGNOSIS

If parotitis is not discernible and the patient is acutely ill with some neurologic disorder suggestive of meningitis, encephalitis, neuritis or myelitis, the physician may find himself in a quandary. He will go far in making the diagnosis by keeping in mind the possibility of parotitis and the knowledge of possible contact. The finding of sterile spinal fluid with a lymphocytic pleocytosis and a slow pulse rate in the presence of fever will help. A number of other conditions, such as poliomyelitis, tuberculous meningitis and syphilis may manifest the same symptoms. If no other findings are available, it will be necessary to await further developments. Uveoparotitic paralysis, characterized by uveitis, parotitis and polyneuritis, has a chronic course.

Swelling of the parotid glands associated with encephalitis has been described by Babonneix and Hubac;[49] the former condition may have been related to excessive salivation, so often observed with epidemic encephalitis. Gundersen,[50] who observed the coincidence of periodicity of epidemic encephalitis and parotitis in Norway, suggested that the two diseases may be related.

SUMMARY AND COMMENT

The incidence of involvement of the nervous system in epidemic parotitis, according to different authors, varies from 1 to 100 per cent. Whether the same agent is responsible for both the parotitis and the neurologic phenomena or whether the former illness activates a virus already existent in the nervous system, as is maintained to be the case, for example, in vaccinal encephalitis, is not known. The findings obtained on serial and repeated spinal punctures, suggesting that the nervous system is involved in most cases, and the observation that the neurologic phenomena may precede the parotitis, militate against the latter view, which, at present, is so popular in explaining the neurologic complications of many other acute infectious diseases.

Necropsy studies are few; aside from the demonstration of meningitis, one may as well concede that little if anything is known of the underlying pathologic processes.

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49. Babonneix and Hubac: Encéphalite léthargique mortelle avec tuméfaction parotidienne bilatérale, Bull. et mém. Soc. méd. d. hôp. de Paris **1**:732 (May 20) 1921.

50. Gundersen, Edward: Has Lethargic Encephalitis Any Relation to Epidemic Parotitis? J. Infect. Dis. **41**:257 (Oct.) 1927.

Clinical Notes

PSYCHOSES ASSOCIATED WITH PROBABLE INJURY TO THE HYPOTHALAMUS AND ADJACENT STRUCTURES

Effects of Solution of Pituitary and Pitressin Given Intraspinally

MILTON L. MILLER, M.D., TOWSON, MD.

The occurrence of diabetes insipidus, obesity and hypersomnia in association with emotional and psychic disturbances has attracted the attention of neurosurgeons. Fulton and Bailey,[1] in a thorough review of the literature, including a report of several cases of their own, pointed out that obesity and polyuria frequently occur in tumors involving the infundibulum. Hypersomnia, in some of their cases, seemed associated with tumor involving the floor of the third ventricle as well as the infundibulum. Cushing [2] described a "hypersomnic" form of tumor involvement of the floor of the third ventricle by gliomatous lesions. Not infrequently in these cases there are encountered emotional and psychic disturbances of varying degree which may appear as outbursts of temper, persistent irritability, confusion, marked loss of memory, confabulation, bizarre behavior, habit deterioration, etc.

Two cases are reported in which the patients exhibited psychotic manifestations sufficient to cause them to be segregated in a hospital for mental diseases. In addition, they exhibited signs of probable damage to the hypothalamus and adjacent structures, such as the infundibulum and floor of the third ventricle.

REPORT OF CASES

The first case of diabetes insipidus, hypersomnia and obesity is reported because of the long-standing deteriorating psychosis, marked at its onset by what appears to be an abrupt personality change, some years after the beginning of the diabetes insipidus.

CASE 1.[3]—*History.*—A housewife, aged 56, entered the hospital on Nov. 28, 1932, because of psychotic behavior which made segregation necessary. She had been unusually well until 1918, when she had a mild form of influenza from which she recovered without incident. In 1920, when she was 43, there occurred the menopause. In 1921, at the age of 44, she suddenly began to drink large quantities of water. The husband said that she placed a 2 gallon bucket of water beside

From the Sheppard and Enoch Pratt Hospital.

1. Fulton, J. F., and Bailey, Percival: Tumors in the Region of the Third Ventricle: Their Diagnosis and Relation to Pathological Sleep, J. Nerv. & Ment. Dis. **69**:1, 145 and 261, 1929.

2. Cushing, Harvey: Papers Relating to the Pituitary Body, Hypothalamus and Parasympathetic Nervous System, Springfield, Ill., Charles C. Thomas, Publisher, 1932.

3. Reported at the Baltimore Medical Society, Neuropsychiatric Section, March 9, 1933.

the bed every night and had emptied it by morning. She voided from ten to twenty times at night and somewhat less frequently during the day, and soon developed an excessive craving for sweets. In 1923, when she was 46, the menses returned for five months. With their cessation the thirst and urinary frequency seemed to increase. There was a gradual but marked increase in weight, so that by 1925 she weighed approximately 250 pounds (113.4 Kg.).

For ten years she complained of mild, dull headache associated with a sensation of pressure, often localized over the vertex. In 1925, because of the complaint of pain across the eyes, they were examined, and the glasses which she had obtained at the age of 30 were found to be adequate.

For some months preceding the change in personality, which occurred in 1926 and which will be discussed later, there were occasional periods of edema of the ankles, without dyspnea or cyanosis. There was also some tremor of the hands and knees, which disappeared after a short time.

The first personality change, growing irritability, was noticed by the husband and confirmed by the son in January, 1926, shortly after it was discovered that

Fig. 1.—From left to right, the patient in case 1 at 18, 39 and 41 years of age.

several thousand dollars over which she had control had disappeared. The family never discovered what had happened to the money. The patient became irritable, and at times depressed and tearful. The husband and son reported loss of interest in friends, cessation of church attendance and gradual indifference to the management of home and family finances, whereas formerly she had been an efficient manager and an ardent church woman, well liked by the townspeople.

For years she had had periods of somnolence, falling asleep frequently during the day and, as her husband said, "right when you were talking to her." In the past few years, the somnolent periods had become considerably less frequent and of shorter duration.

She showed rather marked dilapidation of personal habits, it being difficult to get her to bathe. This behavior was in contrast to her former insistence on cleanliness of person and of home. The family noticed that she had considerable loss of memory for neighborhood and family events, in both the remote and recent past. She rarely forgot, however, requests for candy when her son was going to town for the day. About six or seven years ago, the son said, for a short period she seemed more agitated and somewhat more confused.

In 1929, the patient entered the University of Maryland Hospital complaining of "falling of the womb." Examination showed rectocele, cystocele, complete

uterine procidentia, a small ulcerated area on the cervix, which bled easily, and moderate arteriosclerosis of the eyegrounds without other physical findings. Anterior and posterior colporrhaphy and amputation of the cervix were done. During her stay it was noted that her memory and orientation were poor and that she seemed confused. She acted peculiarly, was rambling in her talk and was suspicious of those about her. She showed a tendency to hoard papers and other things about the ward. At discharge, after a few weeks, she had lost 30 pounds (13.6 Kg.), but soon regained this weight at home.

After that time she frequently expressed suicidal ideas, but never made any actual attempts. For two or three weeks preceding admission, she often threatened her husband with physical violence, and at times actually attacked him. She became very resentful of any opposition to her wishes and extremely difficult to manage.

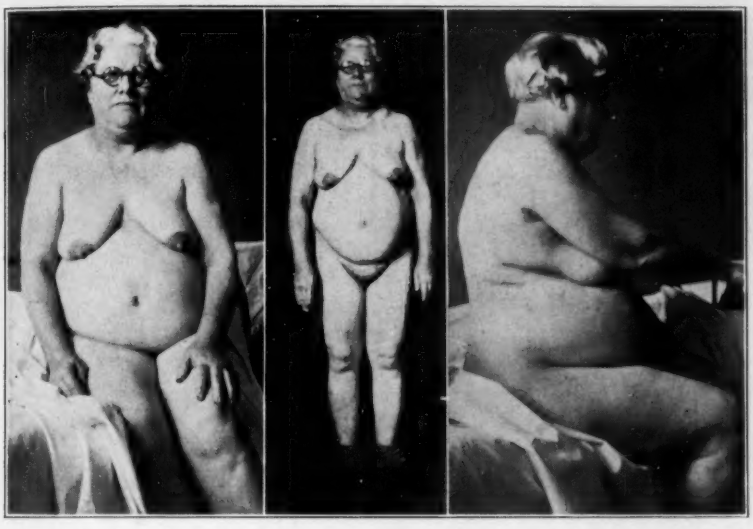

Fig. 2.—The patient in case 1 as she appeared in the hospital.

On admission to the Sheppard and Enoch Pratt Hospital, she complained of excessive thirst and immediately drank a large quantity of water. With a daily output and intake of between 5 and 9 liters, she voided as much as from 1 to 1.5 liters at one time, and urinated from ten to twelve times during the night and from fifteen to twenty times in the twenty-four hours. The administration of solution of pituitary or pitressin by the subcutaneous route considerably diminished intake and output, as illustrated in figure 3.

Physical Examination.—There was considerable obesity, particularly in the trunk; the weight was 228 pounds (103.4 Kg.) and the height, 5 feet and 2 inches (157.5 cm.). The hair of the head was coarse; pubic and axillary hair was scanty, but feminine in distribution. The thyroid was not felt. The breasts were somewhat small. The blood pressure averaged 130 systolic and 90 diastolic in the right arm, and 120 systolic and 80 diastolic in the left arm. Abdominal examination was unsatisfactory because of the obesity. Except for slight blurring of the nasal margins of the disks, the eyegrounds were found to be normal on repeated examination. The visual and color fields also were normal. There was slight pitting

edema of the ankles. Repeated neurologic examinations revealed no abnormalities. Vaginal and rectal examination showed slight cystocele and rectocele.

Laboratory Data: The specific gravity of the urine varied from 1.001 to 1.006; no sugar, albumin, casts or cells were found; the specific gravity of twenty-four hour specimens averaged 1.004. Examination of the blood showed: white cells, 8,000; hemoglobin, 85 per cent (Sahli); red cells, 4,500,000. Repeated lumbar punctures yielded clear, colorless fluid with an initial pressure varying between 200 and 225 mm. of water. There was a good rise and fall after jugular compression, and the pulse and respiratory oscillations were normal; on microscopic examination there were from 1 to 5 cells; the total protein varied between 28 and 38 mg.; the colloidal gold curve was 1112210000. The Kolmer and Kahn tests were negative.

The nonprotein nitrogen of the blood was 40 and 43; a phenolsulphonphthalein test yielded 55 per cent at the end of two hours. The dextrose tolerance test

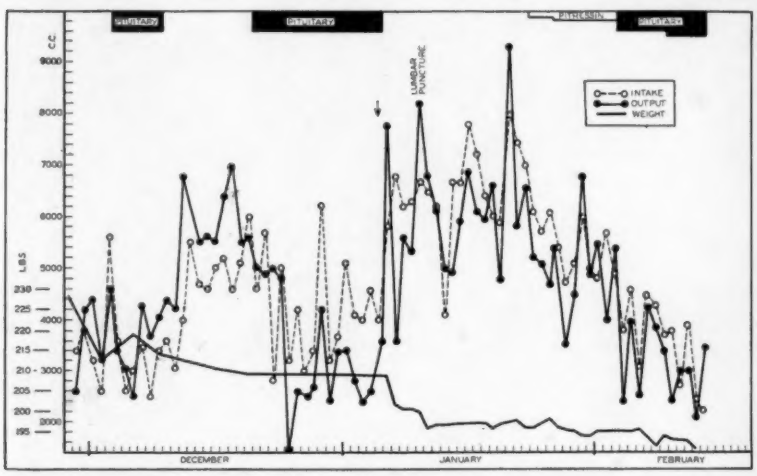

Fig. 3.—The course of diabetes insipidus with treatment by solution of pituitary and pitressin (Parke-Davis). One cubic centimeter of solution of pituitary twice daily was given during parts of December and January, as indicated by the blocks on the chart. The latter part of January, from 1 to 2 cc. of pitressin was given subcutaneously, and 0.5 cc. of extract of the posterior lobe of the pituitary gland, double strength, was administered every six hours during February, as indicated. The solid continuous line represents the weight curve.

(100 Gm. of sugar) approximated a diabetic curve, with a peak of 211 mg. at the end of one and a half hours and 150 mg. per hundred cubic centimeters at the end of two and a half hours. The basal metabolic rate was 7 and 10 per cent. Kolmer and Kahn tests of the blood were negative. Stereoscopic plates of the skull showed no abnormalities of the sella turcica or other findings. Plates of the vertebrae and long bones revealed localized hypertrophic arthritis at the tenth thoracic vertebra.

Mental Status.—Throughout her stay, the patient was often irritable and on occasion when urged to join group activities became combative and resistive and at times struck at the nurses. She was careless in personal habits and insisted on sleeping in her underwear. It was difficult to get her to cooperate in the

measurement of the fluid intake and output. Although she usually drank from four to six glasses of water at one time, she insisted that she never drank more than two. Frequent deliberate misstatement of the amount of water taken was one of her characteristics. She had frequent short crying spells and often complained that nurses and patients were whispering about her and laughing at her. She hoarded old papers in her room and became markedly irritable when they were periodically removed. At intervals she was confused and would be found wandering about the ward trying to find her own room; occasionally she would wake up in the morning asking where she was. Her talk was always characterized by considerable circumstantiality, and often she was seen muttering. She showed considerable memory change, especially in the field of remote memory. She could not give her age, the date of her birth or marriage or the ages of her children. Recent memory also showed some impairment. She could not remember for the most part events which led up to her admission to the hospital. Although she could never give the current date correctly, she managed to keep track of the approximate amount of time she spent in the hospital.

For a few weeks coincident with the discontinuance of routine activities and the regular administration of solution of pituitary she showed some improvement in behavior. She became better able to cooperate with the various procedures, was more agreeable and sociable and had fewer crying spells. With improvement in sleep, following therapy, she dozed much less during the day and had fewer outbursts of temper. During the latter part of her stay her behavior became much like what it had been during the first few weeks. Because of the markedly dilapidating nature of the psychosis, a neurologic surgical consultant thought ventriculography inadvisable.

The next case is reported because of the sudden onset of diabetes insipidus, followed two and a half years later by a frank psychosis with cessation of the polyuria and improvement in the mental status.

CASE 2.—*History.*—A physician's wife, aged 38, was admitted to St. Elizabeth's Hospital, Washington, D. C., on Aug. 2, 1927, in a state of intense excitement. She was born and educated in Mississippi. She was the seventh of eight children and showed no unusual traits during childhood and adolescence, except for an unusual interest in religion. With two other sisters she entered a nurse's training course, and on the outbreak of the war went to France as an army nurse. After a few months of service she married. On her return in 1919 the father noticed that she seemed somewhat depressed and that her complexion had darkened considerably. She was in excellent health until January, 1925, when she had a scanty menstrual period and passed some clots. A few days later, she suddenly became extremely thirsty and for the next two and a half years her intake and output averaged between 6 and 9 gallons daily. During this period she received solution of pituitary, with some diminution in the polyuria. Repeated roentgenograms of the skull, lumbar punctures, examination of the eyegrounds and neurologic examinations gave completely negative results. During 1926 and 1927, she received a series of roentgen treatments over the pituitary body, which seemed to improve the diabetes insipidus.

On Dec. 21, 1926, she was delivered of a dead child by cesarean section. On several occasions, after the onset of the polyuria, the husband observed convulsive seizures accompanied by cyanosis, salivation and vomiting.

In June, 1927, following a dinner party, the patient became tense and excited over the loss of a vanity case belonging to one of her guests. She began to have exalted ideas of a religious nature, was fearful of floods, etc., and because of her

disturbed behavior was sent to the East Louisiana State Hospital in July, 1927. During a few weeks there she postured a good deal, was often mute, had to be fed by tube and was frequently combative. She was transferred to St. Elizabeth's Hospital in August, 1927, with a diagnosis of manic-depressive psychosis, manic phase.

For some time, because of lack of cooperation and combativeness, it was difficult to measure the intake and output. The following table is taken from the record:

	Intake Cubic Centimeters	Output Cubic Centimeters
October, 1927.....	5,530	4,416
	5,190	4,140
December, 1927.....	2,000–3,000	2,000–3,000
October, 1928.....	5,150	4,400

By May, 1930, without treatment, the intake and output apparently dropped to normal and have remained so. Frequent examinations of the skull, eyegrounds and the central nervous system have failed to reveal any abnormalities. Examinations of the urine revealed absence of sugar and albumin, and a low specific gravity until 1930.

For a time during her stay at St. Elizabeth's Hospital she was mute, had to be fed by tube, had hallucinations and was delusional, manneristic and assaultive. During the past two years she has improved to the point where she is permitted to shop in town, attend the theater and assist with work in the hospital. My examination of her mental status showed that she was somewhat suspicious, that she did not acknowledge her marriage, and that she denied her illness. No defect of remote memory was found. Memory of her recent illness seemed correct as to time, but she could not recall many details. A diagnosis of dementia praecox, catatonic type, was made at St. Elizabeth's Hospital.

THE EFFECT OF SOLUTION OF PITUITARY AND PITRESSIN WHEN INTRODUCED INTO THE SPINAL CANAL

The effect of solution of pituitary and pitressin when injected into the ventricle was found by Cushing [2] and his co-workers to be somewhat different from that when it is administered subcutaneously or intravenously. Thus, they produced vasodilatation, particularly of the face and neck, profuse perspiration, retching and vomiting, salivation, a marked fall in body temperature and a lowering of the basal metabolic rate. The effect of these preparations when introduced into the spinal canal has apparently not been reported.

In case 1, the patient was given pitressin and solution of pituitary intraspinally to see what, if any, effects might be obtained which could be compared with the observations noted when it was injected into the ventricle. The protocols follow:

Protocol 1.—One cubic centimeter of pitressin (Parke, Davis & Co.) was diluted in 10 cc. of physiologic solution of sodium chloride and introduced into the fourth lumbar space after 10 cc. of spinal fluid was withdrawn. This was done at 12:05 p. m.

The observations show that there was a drop in temperature of 1 degree one hour after the injection, followed by a rise to 99.2 F. two and a half hours afterward. The temperature then slowly dropped to normal. The blood pressure did not vary significantly. The intake and output of water dropped from a previous average level of from 5 to 6 liters (during a period without treatment) to an aver-

age of 2,300 cc., followed during the next twenty-four hour period by a rise almost reaching the preinjection level. Previous lumbar punctures had had little effect on the polyuria. Nausea, vomiting and abdominal pain did not occur. The only symptom noted was rather marked drowsiness persisting for some hours.

TABLE 1.—*Results Following Injection of Pitressin*

Time	Blood Pressure		Temperature	Pulse	Respiration		Intake	Output
	Right	Left						
12:30 p. m.	118/70	118/78	98.6	70	20	For 24 hours		
1:00 p. m.	.....	.....	98.6	72	20	following		
1:30 p. m.	.....	.....	97.4	70	18	injection	2,300	2,300
2:00 p. m.	120/70	130/70	97.4	76	20			
3:00 p. m.	.....	115/65	99.2	80	20			
4:00 p. m.	.....	.....	99.0	80	20			
5:00 p. m.	110/78	100/66	99.2	80	20	For succeed-		
6:00 p. m.	118/68	110/74	98.8	84	20	ing 24 hours	4,300	5,800
7:00 p. m.	118/66	100/68	98.6	80	20			
8:00 p. m.	.....	.....	98.4	84	16			
9:00 p. m.	.....	.....	98.4	74	16	The 3d day	5,400	6,100
10:00 p. m.	.....	.....	98.4	82	16			

TABLE 2.—*Results Following Injection of Extract of Posterior Lobe of Pituitary Gland, Double Strength*

Time	Temperature	Pulse	Blood Pressure		Symptoms
			Right	Left	
11:20 a. m.	....	..	118/75	105/70	
11:30 a. m.	98.4	86	.....	.....	Complains of numbness of left leg
12:00 m.	98.4	84	118/70	110/78	
12:30 p. m.	98.2	76	112/68	118/78	Drowsy
1:00 p. m.	98.4	72	120/74	118/80	Considerable nausea
1:30 p.m.	98.8	80	110/80	120/82	Patient stuporous, vomited
2:00 p. m.	....	..	.....	.....	Nausea continues
2:15 p. m.	98.6	76	112/80	120/80	Complaining of hot flushes, perspiring face, vomiting, drowsy; observation showed flushing of face and neck
2:30 p. m.	98.6	76	122/78	118/80	
3:00 p. m.	98	80	122/80	124/84	Perspiring profusely; nausea and vomiting
3:30 p. m.	97.4	78	120/78	120/80	
4:30 p. m.	97	76	120/78	124/84	Moderate nausea
6:00 p. m.	98	..	.....	.....	
8:00 p. m.	....	..	.....	... ..	Nausea and flushing disappeared.

Protocol 2.—A few days after the first injection, 1 cc. of extract of the posterior lobe of the pituitary gland, double strength, was introduced, in the same manner, into the spinal canal. Before the injection, the temperature by mouth was 99 F.; the blood pressure was 118 systolic and 90 diastolic in the right arm, and 100 systolic and 70 diastolic in the left arm; the pulse rate was 76 and the respiratory rate 20. The injection was made at 11 a. m.

The intake and output for the twenty-four hours following injection dropped from a previous level of from 5 to 6 liters, to 2,440 and 1,450 cc., respectively. During the next twenty-four hours it rose to 4,700 and 4,300 cc. The nausea, vomiting, perspiration and flushing of the face persisted for several hours; it did not occur after the injection of pitressin. No complaint was made of abdominal pain or griping. The pulse and blood pressure showed no significant changes. The temperature dropped to 97 F. five hours after the injection. During the evening following the injection, the patient was comfortable and symptom-free.

SUMMARY AND CONCLUSIONS

The association of symptoms produced by injury to the hypothalamus, the adjacent infundibulum and the floor of the third ventricle with emotional disturbances is not infrequently found to be due to tumor in the region. Cases of long-standing deteriorating psychosis, as in case 1, preceded by diabetes insipidus, obesity and hypersomnia and without subsequent visual changes to date are not frequently found in the literature.

The abrupt onset of the personality change five years after the onset of the diabetes insipidus and change in weight is of considerable interest.

Case 2 presents only one of the symptoms of injury to this region, namely, polyuria. It preceded the onset of the psychosis by two years and then disappeared with evidence of gradual improvement in the mental status. Obesity and hypersomnia were never present. No other similar cases have, as far as I am aware, been reported.

The intraspinal introduction of pitressin appears to be without much effect, except for reduction in the intake and output of water. The intraspinal introduction of extract of the posterior lobe of the pituitary gland, double strength, appears to have an immediate marked effect on the output and intake of water, to produce marked reactions of flushing of the face and neck, nausea and vomiting and to have some mild influence on body temperature.

Therefore, there appears to be a striking similarity between the systemic reaction produced by intraspinal injection of extract of pituitary and that noted by Cushing and his co-workers following intraventricular injection.

STATUS MARMORATUS RELATED TO EARLY ENCEPHALITIS

THEODORE J. CASE, M.D., ANN ARBOR, MICH.

In 1920, C. and O. Vogt [1] reported eight cases in which a peculiar syndrome appeared soon after birth. Spasticity, athetoid movements, various extrapyramidal symptoms and frequently paralysis were noted. The striking and most characteristic patho-anatomic feature was revealed by the myelin sheath stains, which showed in the striate bodies a network of apparently new myelinated fibers forming a dark interlacing meshwork, in the interstices of which lighter areas were seen. The gross appearance in the Weigert sections was, because of this extra myelinization, not unlike marble, and for this reason the condition was called by the Vogts status marmoratus. Subsequently, Bielschowsky,[2] Meyer [3] and Scholz [4] reported similar cases. In this country attention has only recently been called to this condition by the paper of Löwenberg and Malamud,[5] in which three histologically examined cases and one living patient are described. Like the cases cited in which the authors found an encephalitic etiology rather than the developmental anomaly given as the basis for this condition by the Vogts, it is believed that the case reported here arose on an encephalitic basis.

REPORT OF CASE

Clinical History.—G. D., a white boy, was born on Nov. 14, 1928. The parents were said to be Greek immigrants, about whom little is known. The father was an unskilled laborer, said to be syphilitic, but on this point and concerning the changes in the blood of the mother there are no definite data. The patient was the third of four children, the others being described as healthy. There were no deaths or miscarriages. The average time between the mother's pregnancies was one year. At the time of the birth of the child the father was 40 and the mother 27. The patient was born at full term, by normal labor, and natural delivery. The weight at birth is unknown. The infant was breast fed for the first thirty-five days, when a formula was prescribed.

Coughing and choking spells were said to have occurred ever since birth, especially at night. In December, 1928, the child was hospitalized with severe choking symptoms, and a diagnosis of "thymus gland enlargement" was

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From the Neuropathologic Laboratory of the State Psychopathic Hospital, University of Michigan.

1. Vogt, C., and Vogt, O.: Zur Lehre der Erkrankungen des striären Systems, J. f. Psychol. u. Neurol. **25**:660, 1920.

2. Bielschowsky, M.: Ueber den Status Marmoratus des Striatum, J. f. Psychol. u. Neurol. **31**:125, 1924.

3. Meyer, A.: Zur Auffassung des Status marmoratus, Ztschr. f. d. ges. Neurol. u. Psychiat. **100**:529, 1926.

4. Scholz, W.: Zur Kenntnis des Status marmoratus, Ztschr. f. d. ges. Neurol. u. Psychiat. **88**:355, 1924.

5. Löwenberg, K., and Malamud, W.: Status Marmoratus: Etiology and Manner of Development, Arch. Neurol. & Psychiat. **29**:104 (Jan.) 1933.

made; he received five roentgen treatments over the region of the thymus. In January, 1929, when 2½ months old, the patient was admitted to the University Hospital at Ann Arbor with a complaint of enlargement of the thymus gland.

Physical Examination.—The baby was marasmic, with a continuous weak, whining cry, and appeared to be acutely ill. The weight was 6½ pounds (2.9 Kg.), the height, 21 inches (53.34 cm.). The forehead was asymmetrical, appearing to bulge on the right side, with a depression in the midline; the fontanels were open. The eyes were normal, with prompt pupillary reactions. The respiration was peculiar, with periods of apnea sometimes lasting as long as ten seconds; at times breathing was difficult and audible, with crowing. The reflexes were slightly hyperactive—none was pathologic. Roentgen examination revealed a normal skull and no enlargement of the thymus. The Kahn test of the blood was negative on two occasions. The blood serum calcium and phosphorus were normal, and roentgenograms of the long bones showed no evidence of rickets. The tuberculin test was negative.

Course.—After adjustments in feeding the child seemed to improve and was sent home, but he returned on several occasions for respiratory infections; on two of these occasions he had temperatures of 103.4 and 105 F. and was considered acutely ill. At these times diagnoses of infantile cerebral paralysis and probable idiocy were made.

The patient was admitted to the Michigan Home and Training School in March, 1932. Results of the examination there gave the impression of idiocy. The head was of the microcephalic type. The reflexes were active. No definite paralysis of the extremities was demonstrated, but no purposeful movements of the legs were observed. The child, aged 3 years and 4 months, could neither walk nor talk, was unable to feed himself and was in no way cooperative. The Kahn test was again negative. Tests showed a mental age of 6 months, with an intelligence quotient of 15 (Kuhlman).

On June 15, 1932, death occurred from pneumonia.

Summary of Clinical History.—A child born normally, of apparently healthy parents, appeared to be fairly well during the first month of life, was subject to choking spells and respiratory infections during the next two months, and at 2½ months was marasmic, underdeveloped and considered to be acutely ill. This illness cleared up but was followed by several subsequent acute infections, during one of which the temperature reached 105 F. The child remained conspicuously underdeveloped during the next two years, never achieving voluntary movements of the legs, never learning to walk or talk, remaining totally uncooperative, and at 2½ years of age reaching a mental age of only 6 months.

Pathologic Condition.—Autopsy revealed the dura adherent to the skull cap, especially at the vertex. There were partially organized thromboses in the longitudinal and lateral sinuses and in one of the large pial veins. There was complete absence of the left kidney, and the right kidney was moderately lobulated.

Gross examination of the brain showed the convolutions to be fine and atrophic, but of normal outline. The white matter was narrow and strikingly white. The basal ganglia were penetrated by numerous white scars and stripes, especially in the caudate nuclei and thalami. There was widespread scar production, especially in the brain stem and subthalamic region. Many scars were present in the cerebellum. In the right parietal region the leptomeninges were thickened and fibrotic, forming a focus as large as a twenty-five cent piece. Through this region ran a large, entirely occluded vessel.

Microscopically, the meninges showed slight thickening, with a moderate infiltration of plasma cells and lymphocytes. In places, the meningeal vessels were thickened. Occasional amorphous deposits of calcium were present.

In Nissl sections the cortex as a whole was considerably atrophied, being narrower than is normal. The architecture was moderately well preserved, but the layers were frequently not well outlined owing to the decrease of neurons. Certain deviations from the general histologic picture were observed:

In the frontal region the architecture was moderately well maintained; in this area there was a scar, grossly about the size of a pinhead, extending from the

Fig. 1.—Glial scar in the gray matter; the parenchyma destroyed; the leptomeninges thickened and containing calcium deposits; Nissl stain; Zeiss planar, 20 mm.; projection: ocular 4.

meninges, in which calcium was present, through all layers somewhat into the white matter, and extending for some distance laterally in the fifth layer (fig. 1).

In the central region the second and sixth layers showed an even greater decrease of neurons than did the other layers, though all shared in the loss. The cytoplasm of the remaining nerve cells of the second layer often appeared vacuolated, and many of these cells were distorted into bizarre shapes. There appeared to be an increase in the glia nuclei. The fifth layer contained many small scars and regions in which the cells were either abnormally oriented or disoriented.

In the operculum the individual cells of the lower layers seemed to have no definite orientation; the fourth layer apparently was absent in some places; numerous scars were present in the fifth layer and occasionally in the third.

In the insular region the majority of the neurons appeared disoriented. In many places the third layer was relatively free from nerve cells, giving the appearance of being wider than elsewhere. The neurons of the second layer were likewise scarce.

The occipital region showed the fifth layer definitely scarred in places; near the tip of the occipital pole the architecture was fairly well preserved.

Weigert sections showed a marked decrease of myelinization throughout the cortex. Often the medullated fibers in the molecular layer were fairly well preserved, in contradistinction to the complete demyelinization of the second and third layers. In the lower layers the stubs of the radial fibers and a few of the tangential fibers remained. In the uncus and in the cornu ammonis the myelinization was greatly reduced. Although many scars were present in the cortex, none was myelinated; hence they cannot be called plaques fibromyéliniques.

The putamen was slightly shrunken; the parenchyma appeared, with the Nissl stain, to be essentially normal, except that some of the larger nerve cells were shriveled and pyknotic. Many large, irregular scars containing groups and lines of small round glia nuclei ran here and there through the putamen and were seen to a lesser extent in the caudate nucleus. With the Holzer stain extensive and fairly heavy scarring was seen in the right putamen and caudate nucleus and about the internal capsule (fig. 2). These scars were often lacelike in distribution, with a tendency to concentrate about the blood vessels. The individual fibers were fine and delicate and did not stain heavily. Bielschowsky staining showed no notable increase in the axis-cylinders in the region of the scars, but they appeared to be somewhat increased about some of the blood vessels. In Weigert sections a fairly dense meshwork of apparently new myelinization extended through most of the left caudate nucleus and putamen. This was often in strands and patches, giving in places the appearance of lace. The knots of the meshwork were frequently about blood vessels, forming a stellate concentration of myelinated fibers about these structures (fig. 3).

The pallidum showed no striking parenchymal changes, but a few glial scars were seen with the Nissl and Holzer stains. In Weigert sections it was seen that there was less than the usual amount of myelinization.

The thalamus appeared knobby on its ependymal surface. Its parenchyma was essentially normal in appearance, except for the presence of small glial scars. With the Weigert stain the thalamus was seen to be less heavily myelinated than normal, and in the less myelinated regions the patchy, meshed, abnormal myelinization which was seen in the putamen was also present to some extent.

The subthalamic nucleus and region of the substantia nigra were not remarkable except for the presence of a few scars.

The cerebellum and pons showed no notable changes.

Summary of the Histologic Condition.—There was evidence of an old, fairly prolonged meningitis, with meningeal thickening and calcium deposits; a greatly demyelinated cortex with frequent scars and with destruction of the parenchymatous elements. The basal ganglia, especially the caudate nucleus and putamen, showed many scars in their substance and about the internal capsule. In many places in these ganglia there was a lacy meshwork of apparently new or misplaced myelinated fibers giving roughly the appearance of marble.

The clinical picture of illnesses and infections in this case, preceded by a relatively healthy period, points strongly toward a postnatal origin of the brain involvement.

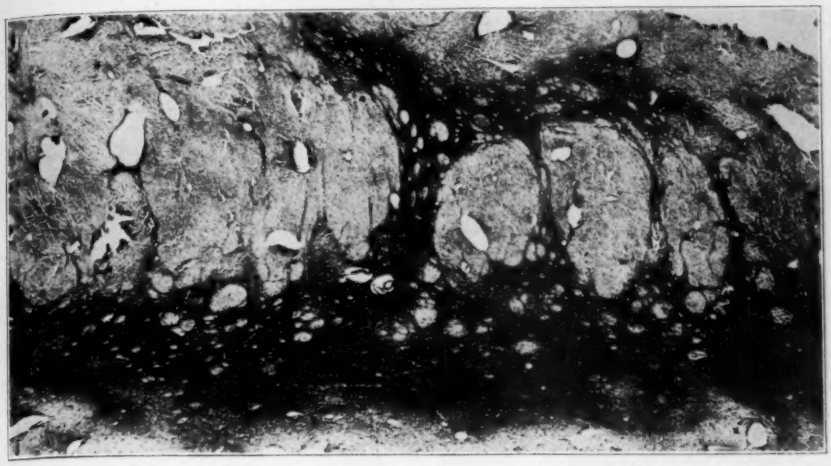

Fig. 2.—Glial scars in the caudatum and putamen; Holzer stain; Zeiss planar, 50 mm.; Bellows, 105 cm.

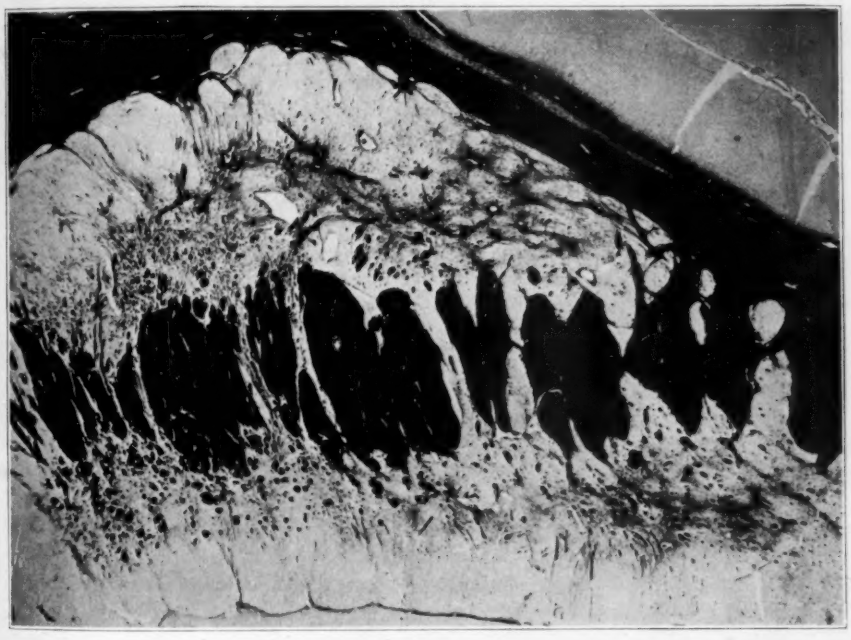

Fig. 3.—Status marmoratus in the putamen and caudatum; Weigert-Kultschitzky stain; Zeiss planar, 75 mm.; Bellows, 105 cm.

COMMENT

The Vogts' original description of status marmoratus considered the disease a developmental anomaly because of its early onset and because they had noticed in some of their cases the presence of a similar picture in other members of the family. The case described by Anton[6] about fifteen years prior to those of the Vogts, having all the characteristic features of this condition, resulted from an acquired process (scarlatina); that of Meyer[3] arose on a basis of vascular disease, probably inflammatory, while the cases of Scholz[4] and of Bielschowsky[2] unquestionably arose on an inflammatory basis. Similarly, Onari[7] emphasized the possibility of a postnatally acquired etiology. The four cases of Löwenberg and Malamud[5] were also found to have developed following an illness which had been preceded by a healthy period.

Histologically, this case shows thickening and calcification of the meninges, with a focal lesion the size of a twenty-five cent piece through which ran a large, entirely occluded vessel; marked parenchymatous destruction of the cortex, with extensive scarification, widespread demyelinization in the cortex, extensive scarification in the basal ganglia, and apparent regeneration of myelinated fibers in the caudate nucleus and putamen. Borst[8] has shown the possibility of regeneration in the central nervous system under similar circumstances. As in the original cases of the Vogts, the extra myelinization seems here to be confined to the striatum.

From the histologic findings it is seen that the picture is one of mild but extensive chronic destruction, apparently an old healed inflammatory encephalitis. In the three cases of Löwenberg and Malamud examined histologically there was likewise an old encephalitis. In this case there was no history of injury at birth and no histologic evidence of hemorrhage. Histologically, then, as well as clinically, my case seems to have an encephalitic background, as do all those more recently described.

In the study of this case an attempt was made to ascertain the nature of a "myelinated scar," and for this purpose successive sections from a given block were stained with Spielmeyer's and with Holzer's stains, and a method was developed for staining a given section with both of these stains. By this means the feathery extramyelinization in the putamen was found not to be in contiguity or association with any scar formation demonstrable with the Holzer stain; conversely, when the scar was most heavy no abnormal or unusual myelinization was visible with Spielmeyer's stain. The apparently new myelinated fibers, like those of other observers, showed many bulbs, loops and evidences of regeneration, and may have grown in response to the loss of other tracts in which scars now are seen. In view of these observations, I am led to conclude, with Hallervorden,[9]

6. Anton, G.: Ueber die Beteiligung der grossen basalen Gehirnganglien, Jahrb. f. Psychiat. u. Neurol. **14**:141, 1896.

7. Onari, K.: Ueber zwei klinisch und anatomisch kompliziertliegende Fälle von Status marmoratus, Ztschr. f. d. ges. Neurol. u. Psychiat. **98**:457, 1925.

8. Borst, M.: Neue Experimente zur Frage nach der Regeneration im Zentral-Nervensystem, Beitr. z. path. Anat. u. z. allg. Path. **36**:1, 1904.

9. Hallervorden, J.: Die extrapyramidalen Erkrankungen, in Bumke, O.: Handbuch der Geisteskrankheiten, Berlin, Julius Springer, 1930, vol. 11, pt. 7.

that the spatial association of myelinization with a glial scar may be incidental; further, that the scarification is the more truly fundamental part of the picture, while the extramyelinization may or may not occur, depending on the age of the patient at the time of the encephalitis and possibly on other factors.

SUMMARY

1. A case is presented which had the clinical history and histologic picture of "marble state."

2. The clinical history and, to an even greater extent, the histologic picture pointed to an inflammatory encephalitic origin for this condition.

3. While both the scars and the myelinization peculiar to status marmoratus were present, they were not found together and apparently had in this case no necessary contiguous relationship.

IDIOPATHIC EPILEPSY IN IDENTICAL TWINS

D. E. McBroom, M.D., Cambridge, Minn., and
Royal C. Gray, M.D., Ph.D., Minneapolis

Ratios ranging from 1 in 80 to 1 in 90 are given for the occurrence of twin births in the new-born population. In the United States [1] for the years from 1920 to 1929, inclusive, the ratio was 1 in 87 and in Minnesota [1] 1 in 78. Muller,[2] Orel [3] and von Verschuer [4] devised formulas for calculating the probability that given twins are identical when data can be obtained concerning certain unrelated physical characters of the twins and their siblings. Weinberg [5] and Knibbs [6] have differential methods for calculating the number of identical human twins. Table 1

Table 1.—*Percentages of Identical Twin Births by Weinberg's Rule*

	Both Male	Both Female	One Male and One Female	Total	Per Cent Identical: Of All Twins	Per Cent Identical: Of Twins of Same Sex
Minnesota	2,343	2,274	2,416	7,033	31.3	47.7
United States	77,043	73,298	74,564	224,905	33.7	50.4

is constructed from the statistics of the United States Bureau of Census [1] for the years 1920 to 1929, inclusive. The figures include white and colored twins, both twins living, one twin living and both twins stillborn.

Monozygotism is commonly predicated on the same chorion, a single placenta and only one corpus luteum. Data on the fetal membranes and placenta are rarely obtainable, and information on the corpus luteum requires histologic examination of the ovaries. Follicles with two or three eggs are sometimes found

From the Division of Nervous and Mental Diseases, University of Minnesota Medical School.

1. Birth, Stillbirth and Infant Mortality Statistics for the Birth Registration Area of the United States, U. S. Dept. Commerce, Bur. Census, 1920-1929, inc.

2. Muller, H. J.: Mental Traits and Heredity, J. Hered. **16**:433, 1925; Methods of Studying Twins, ibid. **17**:195, 1926.

3. Orel, H.: Ueber die Häufigkeit eineiiger Zwillinge, Arch. f. Gynäk. **129**: 719, 1927; Längen- und Massenwachstum von Zwillingen, Ztschr. f. Kinderh. **48**:1, 1929.

4. von Verschuer, O.: Die vererbungsbiologische Zwillingsforschung, Ergebn. d. inn. Med. u. Kinderh. **31**:35, 1927. von Verschuer, O., and Zipperlen, V.: Die erb- und umweltbedingte Variabilität der Herzform, Ztschr. f. klin. Med. **112**:69, 1929.

5. Weinberg, W.: Beiträge zur Physiologie und Pathologie der Mehrlingsgeburten beim Menschen, Arch. f. d. ges. Physiol. **88**:346, 1902; Zur Berechnung der Häufigkeit eineiiger Zwillinge, Arch. f. Gynäk. **133**:289, 1928.

6. Knibbs, G.: Multiple Births, Their Characteristics and Laws Mathematically Considered, J. & Proc. Roy. Soc. New South Wales **59**:128, 1925.

in adult human beings. Von Verschuer,[4] Curtius,[7] Siemens[8] and Cummins[9] raised further objections to this predication. Siemens[8] presented a so-called twelve point dermatologic scheme for determining identical twins. Von Verschuer,[4] Loewy,[10] Spickernagel,[11] Bauer,[12] Klein,[13] Meirowsky[14] and Dahlberg[15] cited exceptions to the scheme. The latter and Variot[16] noted resemblances and dissemblances in configuration of the external ear. Bachrach and Young,[17] Goldberg[18] and Bonn[19] made odontologic comparisons. Gesell[20] and Cathala and Bardy[21] studied the osseous system. Differences in the length and weight of

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7. Curtius, F.: Nachgeburtsbefunde bei Zwillingen und Ähnlichkeitsdiagnose, Arch. f. Gynäk. **140**:361, 1930.

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9. Cummins, H.: Dermatoglyphics in Twins of Known Chorionic History, with Reference to Diagnosis of the Twin Varieties, Anat. Rec. **46**:179, 1930. Cummins, H., and others: Revised Methods of Interpreting and Formulating Palmar Dermatoglyphics, Am. J. Phys. Anthropol. **12**:415, 1929.

10. Loewy, E.: Beobachtungen an Zwillingen, Med. Klin. **21**:1125, 1925.

11. Spickernagel, W.: Ueber ungleiches Haarpigment bei sicher eineiigen Zwillingen, Klin. Wchnschr. **4**:1168, 1925.

12. Bauer, J.: Bemerkungen zur prinzipiellen Bedeutung des Studiums der Physiologie und Pathologie eineiiger Zwillingen, Klin. Wchnschr. **3**:1222 and 2150, 1924.

13. Klein, P.: Zur Frage der Diagnose der Eineiigkeit bei Zwillingsschwangerschaft, Arch. f. Gynäk. **130**:788, 1927.

14. Meirowsky, E.: Erbgleichheit bei eineiigen Zwillingen und Aetiologie der Muttermäler, Virchows Arch. f. path. Anat. **266**:313, 1927.

15. Dahlberg, G.: Twin Births and Twins from a Hereditary Point of View, Inaug. dissert., Uppsala Kungl. Universität, 1926.

16. Variot, M. G.: Note sur la dissemblance des pavillons des oreilles sur deux jumeaux males uni-ovulaires agés de 17 ans, Bull. et mém. Soc. d'anthrop. de Paris **9**:94, 1928.

17. Bachrach, F. H., and Young, M.: A Comparison of the Degree of Resemblance in Dental Characters Shown in Pairs of Twins of Identical and Fraternal Types, Brit. Dent. J. **48**:1293, 1927.

18. Goldberg, S.: Biometrics of Identical Twins from the Dental Viewpoint, J. Dent. Research **9**:363, 1929.

19. Bonn, G. K.: Anthropologic and Odontologic Studies of Twins, Internat. J. Orthodontia **16**:640, 1930.

20. Gesell, A.: Mental and Physical Correspondence in Twins, Scient. Monthly **14**:305 and 415, 1922.

21. Cathala, V., and Bardy, J.: Etude basée sur la recherche des points d'ossification chez les jumeaux univitellins, Bull. Soc. d'obst. et de gynéc. **7**:601, 1928.

twins were extensively examined by Dahlberg,[15] Schatz,[22] Essen-Möller[23] and Wilson and Jones.[24] Newman[25] studied intelligence quotients of identical and fraternal twins. Richmond[26] noted psychic similarity in identical twins. Abt[27] mentioned some unusual resemblances. Galton[28] was the first to recognize the close similarity between the friction ridge patterns of some twins of the same sex. Newman,[25] Wilder,[29] Ganther and Rominger,[30] Leven,[31] Bonnevie,[32] Montgomery[33] and Komai[34] extended his work. Exceptions are given by Cummins and others,[9] Wilder,[29] Poll,[35] Lauterbach,[36] Reichle[37] and Waardenburg.[38] Schiff[39] and Wiechmann and Paal[40] studied the blood groups and Mayer-List and

22. Schatz, F.: Die Gefässverbindungen der Placentakreisläufe eineiiger Zwillinge, ihre Entwicklung und ihre Folgen, Arch. f. Gynäk. **19**:329, 1882; **24**:337, 1884; **27**:1, 1886; **29**:419, 1887; **30**:169, 1887; **53**:144, 1897; **55**:485, 1898; **58**:1, 1899; **60**:201, 1900; **92**:13, 1910.

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26. Richmond, W.: The Psychic Resemblances in Identical Twins, Am. J. Psychiat. **6**:161, 1926.

27. Abt, I. A.: Diseases and Fate of Twins, J. Iowa M. Soc. **14**:395, 1924.

28. Galton, F.: Finger Prints, New York, The Macmillan Company, 1892.

29. Wilder, H. H.: Palms and Soles, Am. J. Anat. **1**:423, 1902; Palm and Sole Impressions and Their Use for Purposes of Personal Identification, Popular Sc. Monthly **63**:385, 1903; Duplicate Twins and Double Monsters, Am. J. Anat. **3**:387, 1904; Palm and Sole Studies, Biol. Bull. **30**:211, 1916.

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Hübener [41] the microcapillary pictures of monovular and diovular twins. Macfarlan [42] reported an instance of identical bearing in identical twins. Beckershaus [43] and Schmidt [44] compared the refractive indexes and other ophthalmometric data on identical twins. Von Verschuer and Zipperlen [4] found great similarity in the form of the heart, diaphragm and thoracic cage in identical twins. Sano [45] observed a remarkable similarity in the disposition of the brain furrows of stillborn monochorionic twins. Imaging or reversal of symmetry in identical twins was reviewed by Schatz,[22] Newman [25] and Lauterbach.[36] Crowden [46] recommended certain clinical observations in determining identity. Various organic disorders and defects occurring in both of identical twins were summarized by Cockayne [47] and Neff.[48] Kalmus [49] attempted to prove a relationship between twinning and nervous diseases.

There are only a few reports in the literature or other available records of epilepsy in both of identical twins. Accounts are given by Herrmann,[50] Toledo,[51] Wilson and Wolfsohn,[52] Olkon,[53] Clausen,[54] Rosanoff and Rosanoff [55] and Talbot.[56] It therefore seems that our cases will be of interest.

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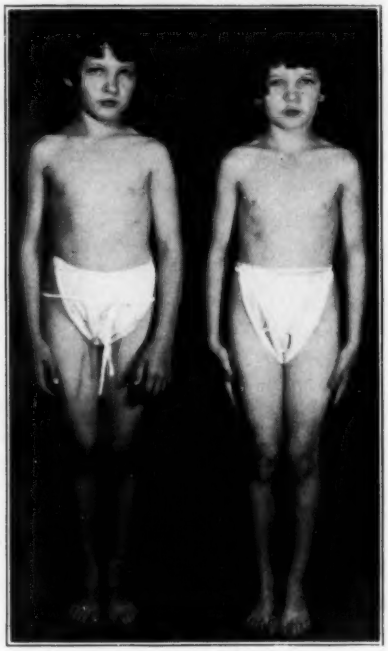

Fig. 1.—Front view (Lucille and Lois).

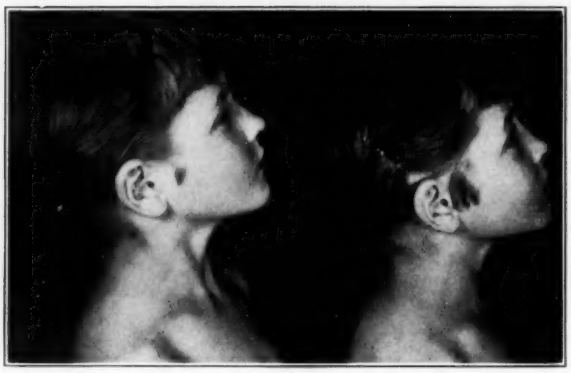

Fig. 2.—Profile view (Lucille and Lois).

REPORT OF CASES

History.—The twins (figs. 1 and 2) were born on April 16, 1924. They were fifth and sixth in order of birth; there were two younger children in the family. The siblings, four brothers and two sisters, were normal. Delivery was in no way unusual, and there was no injury at birth. It is said that the twins had a common placenta and were premature babies. The mother had had two miscarriages, in the third and eighth pregnancies. The father was 42 and the mother 31 at the birth of the twins. The mother was very sick during gestation; otherwise the parents had always been in good health. They were not related, nor were the grandparents. There were no familial diseases, except that one maternal aunt had epilepsy.

There was deficient animation in both of the twins for the first few hours, during which they were not expected to live. They were nursed by the mother for about three months, after which they were fed cow's milk. They apparently grew normally; both were frail although not sickly babies. They sat up, took notice of things, played with toys and began to dress themselves at an earlier age than is usual. Teeth appeared in both at 6 months. Lucille began to walk at 12 months and Lois at 14. Lucille first talked at 14 months and Lois at 16. Neither twin was different from other children of her age, and no peculiarities were noted. They had measles and chickenpox at the same time.

The twins chose for their associates the members of their own family. They were not easily teased by other children. They were accepted as equal by boys and girls of their own age. They were interested in normal play and were apparently as sensitive to pain as other people. Their powers of attention were normal and they were not heedless to danger. They were not abnormally interested in sex and did not lie or steal. They performed ordinary errands similarly to children of their age. The mother checked their outstanding characteristics as being obedience, trustworthiness, cheerfulness and affection.

They had no convulsive attacks of any type previous to the inception of the seizures at approximately 5 years of age. The epileptic symptoms developed suddenly. Lucille (the first-born) had the first seizure, and Lois, the smaller twin, had her first seizure within a week afterward. The seizure was originally characterized by a slight upward tilt of the eyeballs and momentary loss of consciousness. Second similar seizures followed in about one month, and with increasing frequency thereafter. On Sept. 13, 1930, the twins were admitted to the Colony for Epileptics, Cambridge, Minn., as voluntary patients.

At that time the seizures were said to be similar in character and degree and about as first noted. After admission to the colony, Lois' seizures became more frequent and more severe than Lucille's. Lucille's recorded daily seizures averaged three, while Lois' were approximately ten times more frequent. Lucille had only attacks of petit mal; later, during seizures, Lois would fall, have some clonic muscular contractions and a relaxation of the bladder sphincter. Neither twin had any aura; each immediately resumed her activities after the seizure was over. The seizures occurred both by day and by night, and sometimes serially. There was never an attempt at violence. They had no psychic equivalents.

Physical Examination.—The age was 8 years and 5 months. Lois was 49½ inches (125.8 cm.) in height; Lucille, 50¾ inches (128.9 cm.). The weights were: Lois, 53 pounds (24 Kg.); Lucille, 59 pounds (26.8 Kg.). The general development and nutrition were good. General inspection revealed that Lois' shoulders were more sloped; Lucille had a somewhat better, more erect posture; Lois had a wider space between the eyes, and her nose was flatter; Lois had a deeper

philtrum than Lucille; Lois had the nicer lips, Lucille's being slightly pouted; the expressions were different; Lois appeared to be brighter and more like a child, whereas Lucille looked older.

The pulse rate range in a ten day period was: Lois, from 80 to 110; Lucille, from 74 to 104. The rectal temperature range during the same period was: Lois, from 98.6 to 100.6 F.; Lucille, from 98.6 to 100.2 F. The average daily blood pressure was: Lois, 86 systolic and 40 diastolic; Lucille, 90 systolic and 44 diastolic.

The hair, normal in amount and distribution, was practically of the same color, a light brown; Lois' was somewhat finer and more oily, and appeared to be slightly darker; the whorl in Lois' hair was clockwise; in Lucille's, counterclockwise. The eyebrows and eyelashes were the same in color and length.

The skins were of normal color and texture. Lois had many small verrucae simplices on the dorsum of the right hand and a few on the dorsum of the left hand. Lucille had only one on the dorsum of the left hand, and one on the medial aspect of the right knee. Lois had a small scar in the center of the forehead and one over the angle of the left scapula, residuals of chickenpox; Lucille was free from these blemishes. Both children had two small freckles, similarly placed, below the left eye. Lucille had a small, brownish, pigmented spot over the angle of the left scapula at almost the identical site of Lois' scar. Lois had four follicular processes below the right eye; Lucille had no such marks. Each twin had a patch of downy hair over the lumbar spine. The nails were normal in shape; there were no irregularities, and the lunulae were normal.

The extra-ocular muscles were normal. The scleral color was normal. The irises of both girls were blue-gray; there were no distinguishing pigmentary marks. The diameter of the cornea measured: Lois, 7 mm.; Lucille, 7.1 mm. The reactions of the pupils to light and in accommodation were normal. Vision with the naked eye was: Lois, right, 20/30, and left, 20/30; Lucille, right, 20/25 —1, and left, 20/25 —2. Correction to 20/20 was obtained as follows: Lois, both right and left, with +125 +50 at 90; Lucille, both right and left, with +75 +50 at 90. Ophthalmoscopic examination gave negative results. The photographs of their fundi showed no definite similarity in the patterns of the retinal vessels.

The ears differed slightly in shape. Lois' helices were somewhat thicker, and her ears appeared to be larger than those of her sister. The audiograms of the twins were within normal range.

The mouths were normal in size and location, with the differences in the lips previously mentioned. The throats were normal.

The dental descriptions, by Dr. J. T. Cohen, dental research worker, University of Minnesota, are given in tables 2 and 3.

Lois' gums were normal; Lucille's showed mild gingivitis. In general, the condition of Lucille's deciduous teeth was better than that of Lois', which showed large cavities with exposed pulp. The texture of the enamel of the permanent teeth was about the same. As a rule, the eruption of Lois' teeth was slightly in advance of that of Lucille's. Lucille's arch was better developed, and she had a somewhat superior bite.

The glandular systems were normal. The hearts and lungs were within normal limits as to percussion and auscultation. The abdomens were protuberant, but otherwise normal. The osseous systems seemed normal, except that the scapulae tended to be slightly winged. The fingers had the same normal shape. No defect or deformity appeared in any of the extremities. The function of the legs was equal. The gastro-intestinal and genito-urinary systems were normal. Lois occasionally had urinary incontinence during a seizure.

The hand clasps were not constant, sometimes the right and sometimes the left predominating. Both twins were right-handed. Lucille wrote with less hesitancy and in an easier fashion than her sister; her handwriting was more legible than Lois'.

Except as noted in the physical examination, a searching neurologic examination gave negative results in both twins.

The Bertillon measurements in table 4 indicated the close anthropologic agreement of the twins; any difference noted is within the error of measurement.

TABLE 2.—*Dental Measurements*

	Lois	Lucille
Widest lower molar	48.0 mm.	49.8 mm.
Median line, to distal portion of lower right molar	36.9 mm.	38.2 mm.
Widest upper molar	53.4 mm.	54.6 mm.
Median line, to distal portion of upper right molar	42.5 mm.	45.2 mm.
Lower permanent incisors	.....	Slightly larger

TABLE 3.—*Results of Dental Roentgen Examination*

	Lois	Lucille
Upper left deciduous second molar	In place	Lost
Lower left deciduous cuspid	Lost	In place
Upper left permanent second bicuspid	Degree of eruption about equal	
Upper right permanent first bicuspid	More erupted	
Lower left permanent second bicuspid	Erupted; enamel defective	Unerupted
Lower left permanent cuspid	Almost erupted	Less erupted

TABLE 4.—*Bertillon Measurements*

	Lois	Lucille
Length of head	7 1/8 inches	7 2/16 inches
Breadth of head	5 1/2 inches	5 9/16 inches
Length, left middle finger	3 1/8 inches	3 2/8 inches
Length, left forearm	13 1/2 inches	13 6/8 inches
Length, left foot	7 1/4 inches	7 1/2 inches

TABLE 5.—*Results of the Stanford-Binet Intelligence Tests*

	Lois	Lucille
Sept. 13, 1930	96 per cent	95 per cent
Jan. 25, 1932	90 per cent	86 per cent
Oct. 4, 1932	85 per cent	87 per cent

Finger prints made and examined by Mr. Ray Harrington, director of the Minneapolis Police Department Bureau of Identification, showed the left thumbs and left little fingers to be similar in pattern and identical as to ridge count. Lois had seven ulnar loop patterns, and Lucille had eight; the seven patterns appeared in the corresponding fingers of each twin. Thus, there was stronger cross-resemblance between the hands of one twin and those of the other than between the two hands of either twin. The agreement in the prints was not significantly greater than might occur in ordinary siblings; however, this lack of absolute identity does not disprove monozygotism.

The results of the Stanford-Binet intelligence tests, administered by the Division of Research, State Board of Control, are given in table 5.

Complete roentgen examination of the twins, made by Dr. L. G. Rigler, professor of roentgenology, University of Minnesota, showed several pertinent points in common and also several significant points of difference.

The points in common were: (1) bifurcation of the epiphyses of both calcanea; (2) several extra nuclei for the epiphyses of the internal malleoli of the tibias—an unusual variation; there were a greater number of nuclei on the left in Lois and on the right in Lucille; (3) numerous lines of increased density in the lower end of the shafts of the tibias; (4) extra nucleus on the external surface of both patellas—an unusual growth anomaly; (5) a similar development of the pelvis in the twins; (6) pseudo-epiphyses of the proximal end of both fifth metacarpals; (7) a normal scaphoid type of skulls and normal sellae turcicae.

The points of difference were: (1) normal frontal and maxillary sinuses in Lois and slightly developed and much smaller sinuses in Lucille; the maxillary sinuses of Lucille differed in shape from those of Lois; (2) an azygous lobe at the

TABLE 6.—*Measurements of the Hearts*

	Lois	Lucille
Transverse thoracic	22.0 cm.	20.0 cm.
Maximum left transverse diameter	5.9 cm.	5.8 cm.
Maximum right transverse diameter	3.7 cm.	3.0 cm.
Total transverse diameter	9.6 cm.	8.8 cm.
Longitudinal diameter	10.5 cm.	10.7 cm.

TABLE 7.—*Findings in the Spinal Fluid*

	Lois	Lucille
Appearance	Clear, colorless	Faintly cloudy (?)
Pressure, mm. of water	300	300
Cells	None	None
Noguchi test	Negative	Negative
Wassermann reaction	Negative	Negative
Colloidal gold test	0001110000	0001211000
Sugar, mg. per 100 cc.	64.0	65.3

apex of the right lung in Lucille, a congenital anomaly which was apparently not present in Lois; (3) a greater total transverse diameter, according to cardiac measurements, in Lois, the shape of the heart tending to be somewhat globular. The technic of the two examinations differed slightly, which may partially account for these findings.

Summary of the Roentgen Findings: Both twins showed striking similarity in epiphyseal development, in various epiphyseal anomalies and in the appearance of the dense lines in the lower ends of the tibias. The shape and size of the hearts were somewhat different. Lucille had a congenital anomaly, with four lobes in the right lung, which was not present in Lois. The development of the sinuses was distinctly different.

The roentgenograms of the patellas (figs. 3 and 4) illustrate the similarities. Some indication of the differences is shown in the pictures of the hearts and lungs (figs. 5 and 6). A detailed paper on roentgen findings in multiple births will appear later.

The total exposed surfaces of the carpal bones in square millimeters were measured from the roentgenograms: right, Lois, 720; Lucille, 760; left, Lois, 704; Lucille, 740. The average difference between the right and left carpi of a person is 50 sq. mm. The corresponding carpal measurements of the twins were within this average difference.

Spinal punctures were performed under nitrous oxide anesthesia.

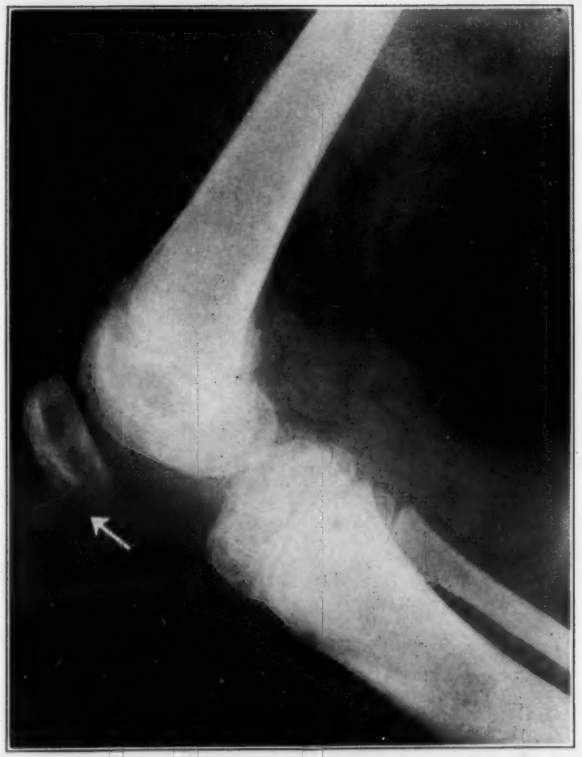

Fig. 3.—Roentgenogram of the right knee (Lois).

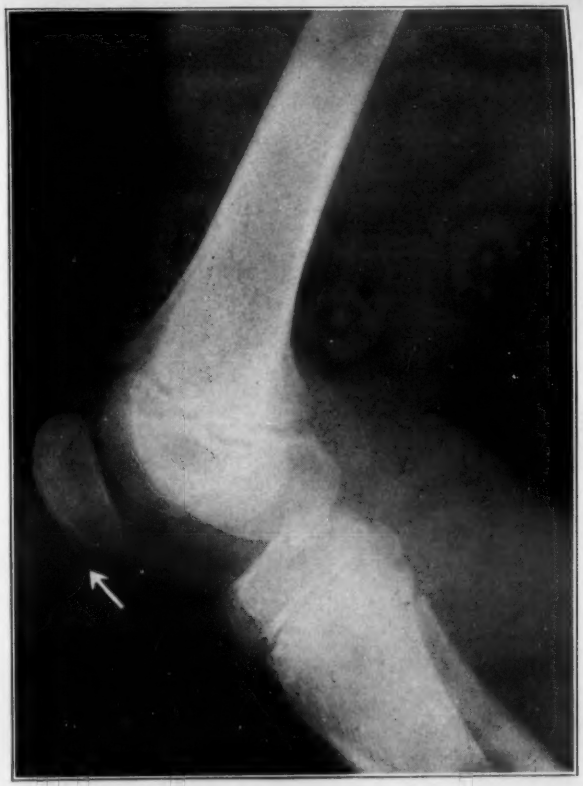

Fig. 4.—Roentgenogram of the right knee (Lucille).

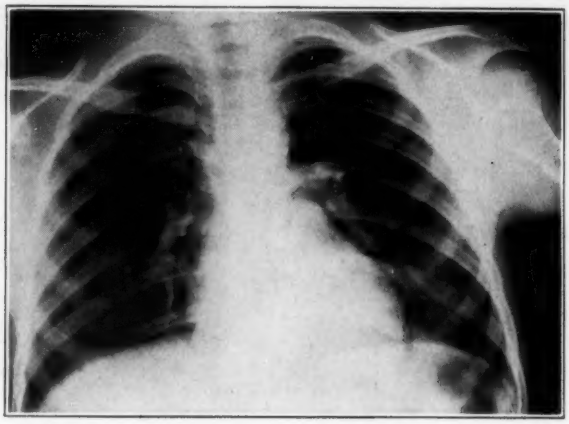

Fig. 5.—Roentgenogram of the chest (Lois).

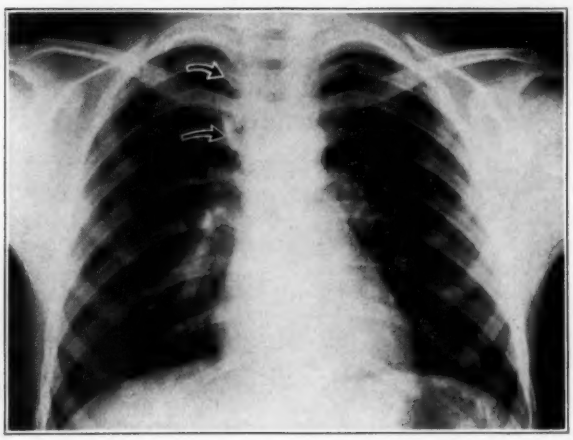

Fig. 6.—Roentgenogram of the chest (Lucille).

Basal metabolic rates were taken on two different occasions. The first readings were: Lois, +23, and Lucille, ±0. The second were: Lois, +17; Lucille, +4.

The results of studies of the blood are given in table 8.

The results of urinalyses are given in table 9.

Personality.—The twins were inseparable and each appeared more interested in the other's welfare than in her own. Their thoughts ran along almost identical lines. It was not uncommon for one to start a sentence and the other to finish it. When asked a question they occasionally answered in unison, using exactly the same words. Though their likes and dislikes were similar, their personalities were somewhat different. Lois tended to be more happy, friendly and appreciative. She

TABLE 8.—*Results of Studies of the Blood*

	Lois	Lucille
Hemoglobin	88	89
Red blood cells	4,780,000	4,650,000
White blood cells	4,650	4,850
Polymorphonuclear cells	62	65
Lymphocytes	29	27
Mononuclears	5	5
Eosinophils	4	3
Calcium, mg. per 100 cc.	11.4	10.16
Phosphorus, mg. per 100 cc.	3.54	3.42
Magnesium, mg. per 100 cc.	1.25	1.20
Wassermann reaction	Negative	Negative
Group	3	3

TABLE 9.—*Results of Urinalyses*

	Lois	Lucille
Specific gravity	1.024	1.027
Reaction	Acid	Acid
Albumin	None	None
Sugar	None	None
Microscopic	Few white and red blood cells	Few white blood cells

was commonly free from fear of the procedures incident to the examination, whereas Lucille was sometimes rather apprehensive and perhaps inclined to be tearful. Lois always seemed eager to do that which was asked of her, and appeared to have better powers of attention and concentration than her sister.

COMMENT

Siemens [8] stated that rare differences in identical twins may be seen with minuteness of examination, and Wilder [29] said that even two hairs, ½ inch (0.5 cm.) long, taken from the same head show microscopic differences. Whereas, as Reichle [37] and Cummins and others [9] indicated, the probability of monozygotism increases with the number of identities in genetically unrelated characteristics, absolute identity becomes impossible with very minute examination. It is logical to believe that persons can never be absolutely identical, because in the continued division of the blastomeres the amount and quality of the chromosomal substance entering into the dividing cells are no doubt never precisely the same.

A single point of similarity is probably without value in establishing identity. Inspection is more reliable than laboratory measurements, and a general summation of resemblances is the best index of monozygotism. This may be especially true in youth, previous to any strongly modifying influence of environment and habits.

SUMMARY

Idiopathic epilepsy in both of identical twins is rarely observed or recorded. The epileptic girl twins reported in this paper are identical, or apparently so in most respects, asymmetrically reversed in some others, and unlike in but few characters. Their general summation of resemblances is so similar that their monozygotic origin seems certain. The association of idiopathic epilepsy and monozygotism is of considerable genetic importance.

ACUTE DIFFUSE (CEREBRAL AND SPINAL) POLYRADICULONEURITIS FOLLOWING ORAL SEPSIS

Probability of Superimposed Infection with Neurotropic Ultravirus of Schwannophil Type

LEWELLYS F. BARKER, M.D., BALTIMORE

During the past two decades, knowledge of infectious processes that involve the nervous system (not only the central but also the peripheral system) has made prodigious progress. Many new clinical syndromes have emerged; the pathologicohistologic changes underlying them have been described, and entirely new conceptions of etiology have become prevalent.

During and since the World War, it gradually became more evident that because of their special characteristics a group of "infectious" polyneuritides must be separated sharply from the general mass of cases of polyneuritis. In England, Holmes,[1] in 1917, described some of these cases carefully under the caption "acute febrile polyneuritis." In France, Guillain and Barré,[2] in 1916, pictured a syndrome (since named the "Guillain-Barré syndrome") of acute radiculoneuritis of the spinal nerves in which there were motor disturbances, loss of tendon and bone reflexes, preservation of cutaneous reflexes, paresthesias, slight objective disturbances of sensibility, pain on pressure on muscle masses and increased protein in the cerebrospinal fluid without increase of cells (so-called "albuminocytologic dissociation"). The onset of the paralysis was usually abrupt, though not so abrupt as in poliomyelitis. The patients grew rapidly worse, and in some instances a fatal termination was feared; however, all recovered (usually much more quickly than from ordinary polyneuritis), so that in later experience Guillain and Barré always gave a favorable prognosis.

Later, similar cases were described by clinicians in Paris, Bucharest and Moscow, but among the cases were some that presented also paralysis of the cerebral nerves and sometimes slight symptoms referable to involvement of the central nervous system and of the meninges. They were believed to be due sometimes to infectious ganglioneuromyositis, and sometimes to atypical epidemic encephalitis with predominant involvement of the peripheral nervous system. Cases of acute ataxia and of acute ascending paralysis of Landry were encountered and were thought to belong to the same groups.

Gradually the idea arose and gained credence that many, if not all, of the cases of the varieties mentioned may be due to infection with ultramicroscopic neurotropic viruses; even when local bacterial infections were found to precede the nervous disease it was suggested that the nervous malady was not due to

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Read by invitation before the Neurological Section of the Pan-American Medical Association, Dallas, Texas, March 23, 1933.

1. Holmes, G.: Acute Febrile Polyneuritis, Brit. M. J. **2**:37, 1917.

2. Guillain, G., and Barré, J. A.: Sur un syndrôme de radiculo-névrite avec hyperalbuminose du liquide céphalo-rachidien sans réactions cellulaires, Bull. et mém. Soc. méd. d. hôp. de Paris **40**:1462, 1916.

bacterial involvement of the nerve structures or to mere intoxication with bacterial poisons but was caused by a complicating infection with a neurotropic ultravirus.

In 1929, a most important study of the effects of certain ultramicroscopic viruses on the nervous system of susceptible animals was made by Nicolau and his associates;[3] the results were published in a long article in the *Annales de l'Institut Pasteur*. These investigators, using the viruses that cause Borna disease, rabies, herpes, neurovaccinia and poliomyelitis, showed that a virus injected into the brain may become generalized throughout the whole central and peripheral nervous system and can be recovered later not only from all parts of the central system, but from the peripheral nerves and the sensory and sympathetic ganglia. Similarly, if the virus is injected into the sciatic nerve it will give rise to the same changes in the spinal cord, nerve roots and root ganglia that follow injection into the brain To express this generalization of the invisible pathogenic agent throughout the nervous system (independent of the site of its entry) with production of manifest lesions in the trunks of the nerves and in smaller nerve branches, Nicolau introduced the term "septineuritis," corresponding to the term "septicemia" used for wide distribution of visible microbes through the blood.

Many have speculated as to the portal of entry of these neurotropic viruses and as to the methods by which they reach the different parts of the nervous system. It has been thought that local lesions in the nose, throat and digestive or urinary tract may give a virus access to nerve endings; thence the virus could go centralward either along the axons of the peripheral nerves or, more probably, along the lymph channels to the central nervous system and to the subarachnoid space and thence, because of the neurotropism and the septineuritic tendency, spread through the whole nervous system, the lesions caused by a particular virus depending on its affinity for special neural structures. Marinesco and Draganescu,[4] though obviously intrigued by the idea of septineuritis in experimental animals, believed that it should not be too hastily applied in human pathology, preferring to await further etiologic and histologic studies for the subdivision of the group of cases of infectious polyneuritis.

The idea of septineuritic spread seems to me to fit well into the picture of acute infectious polyneuritis in man, as will readily be seen from the case here described.

REPORT OF A CASE

History.—E. T. F., a colored man, a portrait painter, aged 22, was admitted, in August, 1932, to the Johns Hopkins Hospital (service of Prof. Warfield T. Longcope), complaining of being unable to talk or to move his arms and legs. Two weeks before admission there were swelling and pain in the left side of the lower jaw, and a week later he felt pain in the neck on movement of the head and began to have tingling in the fingers and toes. Later, the toes became numb, the legs felt heavier and he lost appetite. On the day before admission he suddenly found that he could not use his legs or arms properly and fell when he tried to walk. Gradually also he had lost the power to speak aloud.

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3. Nicolau, S.; Dimanesco-Nicolau, O., and Galloway, I. A.: Étude sur les septinévrites à ultravirus neurotrope, Ann. Inst. Pasteur **43**:1, 1929.

4. Marinesco, G., and Draganescu, S.: Beiträge zum Studium der primären infektiösen diffusen Neuritiden, Deutsche Ztschr. f. Nervenh. **112**:44, 1930.

Physical Examination.—The temperature was 101.2 F.; the pulse rate, 120, and the respiratory rate, 26. The blood pressure was 145 systolic and 90 diastolic. The patient was well nourished, unusually intelligent, cheerful and cooperative. There was flaccid paralysis of all four extremities. He was unable to move the legs at all and could make only flapping, ataxic movements with the upper extremities. There was no paralysis of the face or trunk on admission.

There was an alveolar abscess about the lower left second molar tooth, with swelling of the submaxillary gland on the left side. There was no other glandular enlargement.

There was slight weakness of the left side of the face; the tongue deviated slightly to the right. There were some difficulty in swallowing, whispered voice and weakness of convergence of the eyes, with diplopia on near vision. The deep reflexes were absent in the upper and lower extremities, except that the right triceps, the periosteal radial and the ankle jerks could still be elicited. The Babinski sign was negative. There were loss of sense of position in the toes, hyperalgesia of the feet and hypotonia of paretic musculature. There was no incontinence of urine or feces, but the tone of the rectal sphincter was diminished.

The heart, lungs and abdominal organs were normal. The eyegrounds were normal.

The blood was normal except for a polymorphonuclear leukocytosis (white cell count, 20,400). The urine was normal.

Course in the Hospital.—Several examinations of the cerebrospinal fluid were made. There was some increase of protein (including globulin), but the cell count was never above 10 and in some specimens no cells were seen. The pressure was normal. The Wassermann reaction was negative.

Blood cultures and the Wassermann reaction of the blood were negative.

The infected tooth was extracted, and the alveolar abscess cleaned out. Another infected tooth on the right side was removed. Cultures from the alveolar abscess yielded streptococci and Staphylococcus aureus. Cultures of the cerebrospinal fluid were sterile. Throat cultures and smears were negative for diphtheria bacilli.

On examination of the larynx, paralysis of the left vocal cord was evident.

Frequent neurologic examinations were made. The deep reflexes continued to be absent. The superficial reflexes of the abdomen, the soles and the cremasteric muscles, though absent at first, returned later.

The voice began to improve and, gradually, motility in the extremities grew better. The paralysis of the left side of the face became temporarily more marked, and there was weakness of the right side of the face. The facial diplegia, however, soon passed off.

At the end of two weeks, atrophy of the muscles of the forearms, the hands and the lower extremities began to appear. There was no fibrillary twitching.

Motility was tested frequently by Dr. French, Dr. Bedell and Dr. Ford. By the end of two months, the patient could use his arms much better but could make little use of his legs. After admission there was some weakness of the abdominal muscles, but that soon passed off.

By the end of the third month there were evidences of marked improvement. Though there was still a little weakness of the muscles governing ocular convergence, the facial paralysis had almost disappeared. There was still a little palatal weakness, and the voice was somewhat hoarse. The tongue continued to deviate to the right. Objective disturbances of sensibility were limited to distal

loss of tactile sense and of the sense of position of the fingers and toes. Subjectively, there were hyperalgesia of the feet and tingling. Motility had greatly improved, especially in the upper extremities, though the distal muscles were still somewhat weak, the extensor muscles of the fingers being weaker than the flexor muscles. Movement was beginning to return in the thighs and legs, but distal motility was still much impaired in both lower extremities and the atrophy had increased. The deep reflexes were still absent in the extremities, but the abdominal and cremasteric reflexes had returned. The patient was permitted to be up in a walking machine and to go about for five minutes at a time. Gradually, he became able to take several steps unsupported and later to walk without support.

At the end of five months, practically normal strength had returned in the musculature of all four extremities, the trunk and the face. There was still slight distal anesthesia for tactile and muscle sense. Speech was normal in loudness, though there was a little difficulty in modulation. The tongue still deviated slightly to the right. There was no difficulty in swallowing. The ankle jerks were still absent, but the other deep reflexes had returned. Stimulation of the soles yielded plantar flexion but was felt as a disagreeable sensation which was difficult for the patient to describe. The case was obviously going on to complete recovery with great rapidity.

LOCALIZATION OF THE LESIONS

An analysis of the history of disturbances of sensibility, motility and reflexes shows that there was an outspoken tetraplegia and that for a brief period bilateral hemiplegia was present (because of the facial diplegia, which was transitory). The paralysis was of the flaccid atrophic type, was more marked in the lower than in the upper extremities and in all extremities was more pronounced distalward than proximalward. The objective disturbances of sensibility were relatively slight as contrasted with the disturbances of motility, though there were some distal anesthesias for touch, pain and muscle sense. The special senses were not involved, except for a temporary complaint of loss of taste at the onset of the illness. The deep reflexes were largely lost, but the cutaneous reflexes were only temporarily lost and the Babinski sign remained negative. The psyche was normal, and the cerebrospinal fluid was normal except for albuminocytologic dissociation. Among the cerebral nerves, the first, second, fourth, fifth, sixth, eighth and eleventh were unaffected. The third nerve was unaffected except for slight weakness of convergence and diplopia on close vision. The seventh nerve was affected on both sides, the left more than the right, but only temporarily. The ninth nerve was temporarily involved, with dysphagia. The tenth nerve on the left side was involved in its recurrent laryngeal branch (paralysis of the left vocal cord). The twelfth nerve on the right side was involved, as the tongue deviated to the right. Practically all the spinal nerves were bilaterally affected below the neck, though those innervating the muscles of the trunk were less involved than those innervating the extremities. Temporary meningeal irritation was present on one day when there was a Kernig sign as well as stiffness of the neck; at all other times these symptoms were absent and there was no increase of cells in the cerebrospinal fluid.

Obviously there were multiple lesions of the cerebral and spinal nerves and nerve roots. If there were injuries to the brain or spinal cord they were so slight that they could not be detected clinically.

NATURE AND CAUSE OF THE MALADY

The mode of onset, the course and the rapid recovery (which promised to be complete) point to acute infectious polyradiculoneuritis. How far the alveolar abscess with fever and leukocytosis was concerned in the origin of the neural lesions it is difficult to say. Improvement began promptly after removal of the local infection. The site of the local infection contained streptococci and staphylococci, but these organisms could not be recovered from the blood or from the cerebrospinal fluid. Any effect of the oral sepsis on the nerves must have been through intoxication or through predisposition to infection with some neurotropic ultravirus. The experience of European observers makes the latter idea seem plausible.

If there was an infection with such an ultravirus, it is interesting to consider the possible nature of that virus. Levaditi has attempted to classify the neurotropic ultraviruses that cause diseases of the central nervous system. He has described a "neuronophil" virus, which causes polioneuraxitis (like acute anterior poliomyelitis), and a "microgliophil" and an "oligodendrogliophil" virus which cause leukoneuraxitis (or disease of the white matter of the cord and brain).

It is interesting that Dechaume [5] recently studied cases of polyradiculoneuritis and found that the lesions consist of acute interstitial neuritis, without sclerosis but with perivascular lymphocytic infiltration. There are marked modifications of Schwann's sheath, with proliferation of the cells and an increase in the number of nuclei and with some degeneration of the myelin, though as a rule there is preservation of the continuity of the axons. He described the change as a "true schwannitis," which causes change in the myelin without destroying the axons—a totally different histologic finding from that in ordinary toxi-infectious polyneuritis or in poliomyelitis.

Since the cells of Schwann's sheath in the nerves are homologous with the oligodendroglia of the central nervous system, and since the lesions in these peripheral nerves in acute infectious polyneuritis involve above all the cells of Schwann's sheath, Dechaume suggested that this condition is a "septineuritis due to a schwannophil virus." As the serum of convalescent patients, which is supposed to contain specific antibodies against the virus, is used in the treatment of poliomyelitis, it is possible that one may ultimately find a specific therapy to combat the schwannophil virus.

Though these newer ideas on the etiology of acute infectious polyneuritis are of great interest, one must await further clinical, pathologic, histologic and experimental studies before giving them full acceptance. If such a case should come to autopsy it would seem to me important to attempt experimental production of the neural lesions in a series of animals by injection of material from affected human nerves.

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5. Dechaume, J.: Polynévrite infectieuse ou schwannite à virus neurotrope (documents histo-pathologiques), Rev. neurol. **1**:403, 1932.

SPECIAL ARTICLE

THE TRAINING OF A NEUROLOGIST

WILDER PENFIELD, M.D.,
MONTREAL, CANADA

It promises well for the future of neurology that there is an ever increasing number of young physicians who are turning tentatively toward this specialty, willing to undergo prolonged training. How wisely are they advised as to that training? How often does lack of vision on the part of the adviser clip the wings of the aspirant?

There has appeared in the ARCHIVES a succession of papers which have presented the individual views of outstanding neurologists of different countries on the same subject—the training of a neurologist. In this series it falls to me to speak for the neurosurgeon and possibly to come to his defense!

Complete definition is unnecessary but one may at least distinguish at the start between neurosurgery and that surgery which a general surgeon finds time to execute on the nervous system; for that is too often therapy without understanding. And conversely one should not consider neurology satisfactory when it limits itself to diagnosis and turns its back on treatment, for that is understanding without therapy. If neurology in the broadest sense is to bear its proper share of the burden of modern medicine it must combine understanding with effective therapy and this therapy is, of course, surgical in part only.

In the past, discoveries made in the field of neurophysiology and of neuro-anatomy have cast light at once on diseases of the nervous system. Bacteriology, serology and endocrinology have made their contributions to the treatment of some of these diseases. But because of lack of specialized training, neurologists have often been slow to appropriate and utilize the new facts, allowing others to take over treatment. Furthermore, Horsley, Cushing and a growing school of neurosurgeons have placed in the somewhat unwilling hand of neurology an additional therapeutic weapon.

If the bounds of the specialty are to be extended the training of the specialist must be varied and his knowledge broadened. As a specialty neurology has in the past been formed from various elements: the philosophy of Hughlings Jackson, the inspired clinical insight of Charcot, the reasoned facts of the Dutch school of anatomy, the illuminating cytology of Golgi and Cajal, the early pathologic studies of Alzheimer and Nissl, the experiments of Pavlov and of Sherrington. All these

elements and many others have combined to make neurology what it is. Its future will be determined by the breadth of outlook and the diversity of training of those who enter the field.

It is not possible to give a generally applicable answer to the oft repeated question: "Where shall I study and how long shall I spend on each phase of the work?" The student of neurology must, of course, recognize no national boundaries during his years of preparation and should ignore those national prejudices which he may unfortunately encounter. In other words, he must in his travels take a broader view than do some of the masters with whom he may come to work.

What to study must be given a general answer, although every individual decision must take into consideration the personality and background of the student. It has been customary for a young physician who has completed his general hospital training to sit for a year or two at the feet of some distinguished neurologic clinician and to watch this man label and, in some cases, treat his patients. This is satisfactory as far as it goes, but it is not enough. The young surgeon who enters a neurosurgical clinic for a given period may learn to carry out surgical procedures and to recognize the types of cases encountered there, and that is as it should be; but that likewise is not enough.

In both cases the training, if it stops there, may lead to a narrow outlook and an unproductive life's work because it omits protracted study in the *related basic sciences.*

In addition to the obvious necessity of learning neuro-anatomy, the prospective neurologist or neurosurgeon should study neurohistology, neuropathology, neurophysiology and biologic chemistry. It is not possible to master completely the details of all of these branches, but he should become truly proficient in at least one of these sciences, and this should be done, when possible, before entering the clinical field.

All of this preliminary requirement is the same for neurology and neurosurgery and, further, every neurosurgeon should be a neurologist to the best of his ability, and every neurologist should have a real knowledge of neurosurgery. In a large neurologic clinic the material is different from that of a neurosurgical service, and the methods of examination and localization differ somewhat of necessity. A student should therefore work for a time in both, whatever may be his eventual goal.

If he will become a neurosurgeon he requires additional training in general surgery, for the two fields are interrelated, and if he can arrange it he should have always some association with the operative work of general surgery. No neurosurgeon, in fact, should work alone or be cut off from general surgery and medicine.

But if the neurologist of the future does not choose surgery, he should elaborate one of the fundamental sciences he has studied. This

may be neuropathology in its broadest sense. It may be biologic chemistry used as a method of studying neurologic and even psychiatric cases; and biologic chemistry as an approach to rational endocrinologic therapy promises much. It may be serology and bacteriology with their obvious relationship to neurosyphilis and other infectious diseases of the nervous system. It may be psychopathology as a preparation for treatment of the psychoneuroses. The psychoneuroses will of necessity be studied and treated by both the neurologist and the psychiatrist, and the neurologist who would do this work well should apply himself to certain aspects of psychiatry.

The neurologist and the neurosurgeon must endeavor to enlarge their common field. It will always be necessary for them to subdivide the field from the point of view of therapy and to a less extent in diagnosis. But the neurosurgeon who operates on patients without making his own critical diagnoses may be a surgeon but he cannot be a good one.

As a matter of fact, no neurosurgeon can avoid functioning as a general neurologic diagnostician to some extent, and it is the common experience of neurosurgeons today that rightly or wrongly an increasing number of cases is referred to them directly by general practitioners without decision as to whether the cases are properly medical or surgical. This is true of those neurosurgeons who were originally "medical" neurologists, but it is true also to some extent of those men who began as surgeons.

The training which seemed adequate in the past will not be adequate for the future. Neurology has reached a further stage with a broader scope. New men who would enter this broader field and who would take full advantage of all its opportunities should train themselves thoroughly to do special work in it as physiologists, pathologists, surgeons, biochemists, serologists or psychotherapeutists. With the increase in the number of such men neurology will begin to bear its proper share of the burden of modern medicine.

Abstracts from Current Literature

THE NEUROLOGY OF GALEN: A CRITICAL SURVEY. A. SOUQUES, Rev. neurol. **1**:296 (March) 1933.

This delightful essay brings from the innocuous desuetude in which he has so long reposed the brilliant experimental neurophysiologist whose name meant so much to the medieval world yet fell to such depths after the Renaissance. Truly it has been said that the good that men do is buried with them, and the term galenical is one of opprobium. While it is true that Galen made many mistakes, that he never dissected the human body, that he indulged in vapid controversies, that his theories as to the circulation are almost as bad as his "theriac," yet a keen scholar, digging beneath the dross that has encumbered Galen's teachings, uncovers much pure gold. Indeed, toward the end, Souques apologizes to Galen for having insisted earlier on the eponymic designation of one-sided convulsions as Bravais-Jacksonian, when the credit for their minute description rests with Galen seventeen centuries earlier.

More is known about the life of Galen than of most of the ancients on account of his autobiographic tendencies. His father was a rich senator who cultivated the sciences of that day, a calm, judicious parent. His mother, on the other hand, was a regular Xantippe. Galen inherited his love of study from the one and his love of controversy from the other. The name Galen signifies serene, calm, and Souques suggests that his father Nicos believed in the prophylactic value of names. Galen received a liberal education and turned from the study of philosophy to that of medicine, which he pursued with an ardor that carried him to all the centers of culture and to many parts of the world. Frequently these pilgrimages would be initiated by dreams of his own, or of his father, and one of his last books was entitled "Diagnosis of Diseases by Means of Dreams." Incidentally, Souques believes that Galen was the first formal psychotherapeutist. The school of Alexandria with its magnificent library and its anatomic museum undoubtedly proved stimulating to the young scientist just entering manhood. On his return to Pergamum he was made surgeon to the gladiators and was surprisingly successful in his treatment of injuries of the nerves. Following an uprising, however, Galen, who disliked the idea of dying, established himself in Rome at the age of 32.

In Rome, everything depended on the individual. There were no requirements for practice; every one might practice what he wished, and the medical profession, if it could be called such, was overrun with cults, dogmas and plain ignorance. With his background, Galen soon rose to the front rank, being court physician, and astounded many by his acute powers of diagnosis. With his powerful backing he was able to pursue his experiments without hindrance, both in public and in private, and gained immense contemporary fame. To the jealousies that were engendered he replied in vigorous counter-assaults, and his skill in invective carried him to even greater heights. When words sufficed to keep him whole, he stayed, but when menaced by enemies or by the plague, he fled Rome for shorter or longer periods and retired to write his books. His scorn for his enemies was equaled by his own vanity. With ready pen he wrote long diatribes, as well as essays on philosophy, mathematics, rhetoric, music and archery. However, his fame is better grounded on his medical works, which are numerous and exceptionally well preserved. Souques divides the consideration of his work under three heads: anatomy, physiology and clinical neurology. It is understood, of course, that the author has picked out from the vast writings only those concerning themselves with the nervous system. What he has uncovered, however, should stimulate specialists in other lines to have recourse to the writings of Galen for observations of equal merit in their own chosen fields.

The Anatomist.—"The physician should be a man that dissects," was one of Galen's revolutionary dicta, and he carried this out all his life. Yet he never dissected the human body and, except at Alexandria, never saw preparations of human organs. On two occasions he studied the skeletons of exposed criminals whose bones had been picked clean by vultures. He maintained that the books of his predecessors were so full of errors that they were useless to students, and also made the mistake of affirming that organically all animals, including man, were absolutely identical. Galen dissected all sorts of animals, birds, reptiles and fish, but his most useful preparations were those of monkeys. As applied to human anatomy, therefore, they are far less useful than those (unfortunately lost) of Herophilus or of Erasistratus, who dissected the human body. The dissection of animals is a necessity for those who would operate on men, since only in that way can the surgeon know what he will find when he has exposed the interior.

Galen erred in ascribing different functions to different parts of the nervous system based on their consistency. He thought the brain and the sensory nerves soft, the cerebellum, the spinal cord and the motor nerves hard. Some organs were equipped with both sorts of nerves, the soft supplying the sensory portions, the hard the motor portions. Among the cranial nerves, the facial was the last hard one, the others supplying the viscera; since these were devoid of voluntary movement, they had only soft sensory branches. The cerebrum was the "prince of viscera," but Galen, while describing the convolutions, failed to note the distinction between white matter and cortex. On the other hand, the interior of the brain, the ventricular system, the epiphysis and hypophysis, were considered very important by him. The description of the communications and functions of the ventricles seems especially fantastic to the modern mind. The lateral ventricles communicate directly with the nasal cavities through pores in the nasal mucosa. The third ventricle communicates with the pharyngeal cavity by means of the hypophyseal stalk and gland. In the ventricular cavities is elaborated the psychic pneuma which energizes the brain. This pneuma reaches the cerebellar ventricle by way of the aqueduct (Souques does not agree with Rouget that the aqueduct was not discovered until Sylvius' time) and activates the cerebral nerves. The spinal cord and its roots are described, the cord serving to combine the nerve filaments going to all parts of the body and make for their greater security. Galen described the cervical and lumbar enlargements of the cord, but stated that the cord extends throughout the vertebral column, an error manifestly drawn from the dissection of animals. Only seven cranial nerves are recognized, the olfactory being considered part of the brain. The optic nerves spread out to surround the vitreous, and insert into the lens and are canalized (in this he followed Herophilus) in order to allow the flow of pneuma. Omitting the fourth nerves, which he considered to be tendons to keep the quadrigeminal bodies in place, Galen recognized the difference between the motor and sensory divisions of the trigeminal, omitting only the description of the semilunar and ophthalmic ganglia. His fourth pair consists of the palatine nerves. Inexplicably, the abducens is omitted from consideration. However, Galen separated the facial and acoustic nerves, recognizing the difference in function of the two, but combining them to form his fifth nerve. The sixth nerve of Galen comprises the glossopharyngeal, the pneumogastric and the accesorius and the sympathetic chain as well. Galen described the course and distribution of these nerves, and the superior and recurrent laryngeal branches, enthusing over the marvelous character of the last. He also recognized the three cervical sympathetic ganglia, though he believed that the chain descends from the base of the brain to be distributed to the organs of the body, along with the vagus nerve. Finally, the hypoglossus forms Galen's seventh nerve, and is sharply distinguished from the lingual branches of the trigeminal. Moreover, he recognized the difference in distribution of the filaments, although the division of these branches into those of common sensibility and gustation was to come later. The description of the spinal nerves is considerably better; not only were all accounted for, but many were traced to their ends, and certain nerves, like the

phrenic, were studied in detail. The excellent description, however, is often marred by questions of why and wherefore, the answers to which are often fantastic.

His knowledge of anatomy occasionally helped Galen to make astounding diagnoses. In the case of Pausanias, for instance, whose fingers were treated locally on account of anesthesia, Galen elicited the history of a fall, and located the trouble at the seventh cervical vertebra. He even noted that the sensory and motor roots are different and can be affected independently.

Galen knew the dura and the pia and the subarachnoid space, but was not explicit in regard to the arachnoid membrane. The sinuses served to protect the brain from the skull and also to bring venous blood for its nutrition. The arteries of the brain came off the hexagon at its base and formed the rete mirabile whence flowed the psychic pneuma, but they were also distributed to the brain itself, both over the surface and into the interior, including the ventricles. Only the veins furnished nourishment to the brain, the cardiac left ventricle being concerned with the distribution of the vital spirit to all parts of the body, including the brain. The nutritive or vegetative pneuma had its origin in the liver and was distributed by the venous system.

The Physiologist.—Galen recognized that the brain is the center of movement and of sensibility, that the spinal cord is under its dominance, and that the nerves merely carry the motor and sensory impulses. When he damaged the dura the animal lost neither motion nor sensation; when the cerebrum was involved minor disorders arose, but when the ventricles were opened serious disturbances became manifest. The greatest paralysis resulted from opening the cerebellar ventricle, and the animals usually died. By suppressing all communication between the brain and spinal cord he rendered the animal senseless and motionless. His greatest *tour de force* was cerebral compression. It is questionable whether Galen was fully aware of the contralateral paralysis following cerebral damage; nevertheless, this observation dates back to Hippocrates and may have been considered too common to be worthy of discussion. Galen found no disturbance following median longitudinal section of the spinal cord, but on transverse section he paralyzed the animal below the incision for both motion and sensation. Unilateral section paralyzed the same side. The extent of the paralysis varied with the level of the incision, and high cervical transection killed the animal. Probably he did not observe the sensory changes in the contralateral limb after hemisection of the spinal cord. Section or ligature of the peripheral nerves produced loss of motion and sensation below, but did not interfere with them above the level of interruption. Just as there could be no movement without the nerves, however, the muscles were required for movement. Galen showed for the first time, moreover, that muscles had but a single movement, that of contraction, and decontraction was accompanied by contraction of the antagonist muscles.

The physiology of the brain and of the special senses was based on speculations, some of which were acute, some of which, as Galen himself said, were revealed in dreams, and some of which were inherited from the philosophers. Their intricacies are stated as clearly as possible by Souques. "The reasoning spirit inhabits the brain; it commands voluntary movement, perceives sensations, remembers, imagines, wills, understands and thinks. [Since Galen's cerebral physiology dominated scientific thought until the Renaissance and beyond, Souques' review is quoted.] The pneuma or spirit is a subtle fluid, an aerial breath, which, without being the same as air, nevertheless comes from air. It is breathed in by the lungs at each inspiration. From the lungs it passes to the heart, thanks to the supposed communication between the bronchioles with certain vessels (the pulmonary veins) that bring it to the left ventricle. This elaborates and transforms the pneuma into vital pneuma or vital spirit. This vital pneuma or spirit is not simply pure pneuma but a mixture of pneuma and blood (blood passed from the right ventricle to the left ventricle by imaginary pores in the interventricular septum). At each contraction the left ventricle, the seat of the vital pneuma, thus ejects pneuma into the aorta whence it is distributed by the arteries to all

parts of the body bringing energy and heat. In considering the origin, course and termination of this pneuma, as well as its calorific function, one cannot help thinking of oxygen. Just like the pneuma, the oxygen comes from the air, penetrates into the bronchi, passes to the left ventricle, which, at each of its contractions, ejects it into the aorta whence it is distributed to all parts of the body and produces heat. But Galen did not know about oxygen or the mechanism of internal combustion. Lavoisier was not to come until the eighteenth century.

"The part of the vital spirit which rises in the internal carotids and vertebral arteries is distributed throughout the brain by the retiform plexus and is then elaborated and transformed into animal spirit or psychic pneuma. The vital pneuma, says Galen, 'is carried off by the cerebral arteries. It cannot promptly penetrate the retiform plexus but rather is held in its numerous and varied byways so that, traveling a long distance, it eventually becomes transformed. This completed, it falls immediately into the anterior ventricles of the brain. It would not do for the pneuma to remain too long in the retiform plexus or that it should escape from it still improperly formed.' By what paths does it fall into the ventricles? There is no doubt about it. If 'the psychic pneuma is contained in the whole substance of the brain and not in the ventricles alone,' it is because that which is contained in the ventricles enters into the mechanism of volitional movement and of sensation. These ventricles are at the same time the laboratory for the purification of the spirit and its reservoir. From the anterior ventricles the animal spirit passes to the median ventricle where it is further purified and from thence into the fourth ventricle which transmits it to the nerves. In this process the processus vermiformis or inferior vermis of the cerebellum intervenes as the jailer of the spirit. If this vermis spreads into the canal that leads from the median ventricle to the fourth it plugs the passage and shuts the door to the spirit. On the other hand, when the vermis contracts, it opens the passage. Having come into the fourth ventricle the spirit gains access to the nerves and transmits the motor orders to the muscles, and transmits the sensory impressions from the skin and the sense organs." In a footnote, Souques explains Galen's deductions from some of his experiments. "If the cerebral ventricles are compressed so as to force out all the pneuma they contain, the animal loses motion and sensibility but does not die. As soon as the compression is removed, motion and sensation return with the filling up of the ventricles by new pneuma. One must remember that the reasoning spirit inhabits the brain and that the psychic pneuma serves it in the manner of an instrument for motion and sensation."

"How does the reasoning spirit move?" asks Souques. "By the dissemination of the animal spirit, of which the hard or motor nerves are the conductors. This spirit activates the muscles which contract and produce movement. This explanation," says Souques, "recognizes the facts but does not explain the essence of voluntary movement. It is true, however, that we are no further advanced today. Instead of animal spirit or psychic pneuma we term it neural current, but this is not more satisfying and does not solve the problem any better."

The reasoning spirit perceives sensations always by way of the animal spirit which is conveyed by the soft or sensory nerves. "All the organs of the senses, says Galen, get from the brain the principle for sensation, but among themselves they have specific differences, depending on the nature of their nerves and their sensory faculties. Among these faculties, one discriminates among colors, another among sounds, another among odors. . . ." The organ of smell, he continues, was alone placed within the skull in the anterior ventricles of the brain that contain a vaporous pneuma. Thus the corpuscle that caused the sensation must modify a portion of the brain. The sense organ had to be protected by a membrane that would allow the passage of only the odoriferous particles. Moreover, under certain conditions, this membrane would allow air to pass for the respiration of the brain, while excluding odors. Still further, this membrane allowed the escape of superfluous liquid, pituita, from the brain. Incidentally, the gaseous waste products of cerebral activity rose and escaped through the cranial sutures. Of

this passage Souques says: "Penetration by air, penetration by odors of the cerebral ventricles, expulsion of aqueous waste through the nasopharynx: three ideas, three errors."

However, Galen performed the following experiment. He filled the noses of slaves with odorous substances, and as long as they did not breathe they experienced no sensation. When they did breathe, the sensation became extremely strong. Loss of the sense of smell, when not due to a disease of the brain, was due to stopping up of the pores of the ethmoid.

As regards hearing, Galen expressed himself as follows: "Necessarily there is a prolongation from the brain to the ear for receiving an impression from without. Now, this impression is a noise, a sound produced by air beaten or beating, it matters little as long as it is understood that the impulse set in motion by the stroke, advancing like a wave, should rise to the brain. Nature has given the strongest guarantee possible to the auditory nerves in placing there a hard thick bone pierced by spirals after the manner of a labyrinth. By this precaution, cold air, with all the violence that might have been given it by direct passage, becomes softened little by little by repeated reflections in these sinuous detours. Moreover, nature gave these nerves an appropriate structure, making them as hard as possible. However, if they had been completely hard, while they would have been less vulnerable, their sensibility would have been practically lost."

Galen filled many pages with a discussion of the mechanism of vision and the function of the optic nerves, though he stated that the enigma of the chiasm was explained to him by his "demon" in a dream, but that he was further enjoined from divulging this explanation. The subject of optics was apparently not inconsiderably known to Galen, who discussed the luminous cones, the straight path of a beam of light, refraction and reflection. "The organ of vision," said Galen, "contains a luminous pneuma that comes continually from the brain, and the optic nerves are hollow for the purpose of receiving this pneuma. In the eye the luminous rays, reflected by external objects whose image they carry, meet with this luminous pneuma. And by the action of like on like results a specialized sensation that is carried by the optic nerve to the brain, the brain perceiving the image of the lighted external object."

For sensation to occur two conditions were necessary, according to Galen, an alteration or modification of the sensory nerves and a cerebral perception. Little would be needed today to bring Galen's theories up to date. Even the "external agent," which is now spoken of as vibrations, Galen conceived of as being propagated "like a wave."

As far as thinking is concerned, the reasoning spirit acted by means of material perceived through the senses, a theory later championed by Locke and by Condillac. Probably Galen did not precede Gall in cerebral localization. While he located voluntary movement and sensation within the cerebral ventricles or in their immediate vicinity, he did not believe that the complexity of the brain was significant as regards intelligence, a theory that has been proposed by Erasistratus. The ass, said Galen, has a complex brain but no intelligence; rather, then, explain man's intelligence on the better quality of the psychic pneuma.

The Clinician.—Clinical medicine, for Galen, rested on anatomy and physiology. His formula was "To ask about all the symptoms, present and past, defining each individual symptom, and past symptom, not only of the patient, but of his relations." Once the topographic diagnosis is established, the nature of the lesion remains to be found. The disease might be due to traumatism, cold, heat, dryness or wetness. Paralysis of a single muscle would rule out a lesion of a nerve, since each nerve was distributed to several muscles. On the other hand, cold injured only the affected muscle. Even the disturbances of the sphincters in cases of medullary lesions were known to Galen. In a case of quadriplegia with maintenance of respiration, Galen localized the lesion in the cervical cord, below the nerves that went to the diaphragm.

Galen was familiar with apoplexy, hemiplegia, epilepsy, migraine, amnesia and delirium, all of them being diseases of the reasoning spirit and therefore situated

in the brain. He recognized that death in apoplexy resulted from respiratory paralysis and insisted that intermittent, laborious respiration was the worst sign. [Cheyne and Stokes were preceded by Galen.] Galen differentiated between spinal and cerebral hemiplegia on the basis of facial involvement and knew of isolated paralysis of the ocular muscles, of the tongue and of other muscles. He even differentiated central from peripheral facial paralysis. Aside from the fact that hemiplegia was caused by a focal lesion, Galen's ideas concerning pathogenesis were peculiar. Apoplexy resulted from a cold humor, or a thick or viscous one that filled the ventricles; it was not the effect of a general cerebral dyscrasia as in lethargy, phrenitis and mental disease. Epilepsy was given a good description and was blamed on the ascent of the opening of the stomach toward the brain. Then comes the description of focal epileptiform seizures: "Rarely there presents itself another type of epilepsy as it might be called. The disease begins in a certain part, then mounts to the head while the patient retains his consciousness. While I was still young I saw this phenomenon for the first time in a boy of 13 years; I saw it with the most distinguished physicians of my country, brought together to decide on a method of treatment. I heard the boy tell how the attack began in the leg and how it rose directly upward to the neck by way of the thigh, the iliac region, the side and the neck as far as the head, and that at this juncture, he lost consciousness. When asked about the nature of the substance that rose toward his head the boy was unable to tell. Another young man who was quite intelligent, capable of feeling what went on within himself and more apt at explaining it to others, replied that a sort of cool breeze rose within him. In the first boy the attack started in the leg. The physicians in consultation attempted to cure him. They purged him completely, applied to the leg a mixture of thapsia and mustard and first ligated the member above the starting place of the attacks; and thus succeeded in arresting the attacks which were of daily occurrence." Souques points out that the whole picture of the Bravais-Jacksonian attack is present in the passage cited. [It is probable that Bravais went little further than Galen, but who would say that Jackson had not?] Galen's ideas on pathogenesis were dominated by the current humoral theories. "A thick or viscid humor called phlegm or pituita injures the brain either by changing its temperament or especially in obstructing the conduits of the psychic pneuma which is retained in the ventricles of the brain. The principle of the nerves acts to abolish this unbearable matter and the crisis follows." The relationships between epilepsy and melancholia (deterioration?) were stressed by saying that black bile might be retained in the cerebral ventricles. Galen was in error in attributing local convulsive seizures to a disease of the spinal cord.

Black bile, inundating the whole body of the brain, caused melancholia, just as the atrabile formed by combustion of yellow bile caused wild delirium, with or without fever. Phrenitis, due to pale bile, was associated with milder delirium. However, such persons were not mentally defective, since the delirium disappeared with the fall in fever. In Galen's description of melancholia and hypochondria one may find certain features of psychasthenia with obsessions and phobias: "The melancholiac persons are ever a prey to fears, but their fantastic ideas do not always take the same form. One patient imagined himself made of shells (coquilles) and in consequence avoided all passers-by for fear of being broken. Another, seeing cocks crow while flapping their wings, imitated their movements and their cries. . . . In effect, just as external gloom inspires fear in practically all men, so the color of black bile, obscuring the seat of the intellect, engenders fear."

Headache received considerable space from Galen. Vertigo was due to a hot and vaporous pneuma that reached the brain by way of the arteries, or sometimes, as the result of a dyscrasia, originated in the brain. Migraine was caused by the same type of condition.

Hysteria in Galen's system had nothing in common with that of Babinski or of Charcot. Essentially characterized by respiratory disturbances, it was of uterine origin as indicated by the terms uterine apnea and uterine suffocation, by which it was also known at this epoch. The origin of this disorder was to be found

in the retention of sperm which underwent putrefaction. [This sperm was the normal product of the female organs, since male and female organs were considered to differ only by their location.] Asked how small a quantity could cause such perturbations, he drew comparisons from insect bites, poisons and hydrophobia. Galen did not believe that hysteria was due to distortions or wanderings of the uterus, a common belief until much later.

To Galen one is indebted for the cameo-like definition of medicine: the art of reestablishing and conserving health. Hence, therapeutics were of great interest to him. His wide travels furnished him with all the pharmaceutic lore then in existence, and he collected his own materials for the famous theriac, and combined the sixty-four various ingredients with his own hand. Medication in cases of nervous disorders was scarcely begun, although trephining for epilepsy was frequently performed. The cranial disks were carried as amulets. Hygiene played a preponderant rôle in all therapy, and Galen regulated the hours of sleep and exercise, the diet, baths and other measures. In addition he should receive credit for being the founder of psychotherapy. In his treatise on the passions of the mind he divided people into two groups, those who were sick and those who were not; the latter he left to the moralists while he claimed the field of the mentally sick. While equipping the mentally sick with a sort of mentor and counseling equanimity, he nevertheless sought to treat the mind through the body. This was all the more reasonable since he did not stop with Hippocrates in considering that the soul was influenced by airs, waters and places alone, but also by age, sex, diet and other factors. Just as the reasoning spirit was the brain's temperament, so it might be deranged by external causes, and allowance should be made for this in meting out punishment.

General Appreciation.—Galen's standing has suffered greatly from the many erroneous deductions that he drew from observed facts, and from the unscientific nature of his doctrines. The most serious errors resulted from the fact that he had never dissected the human body. Aristotle was more prudent in drawing deductions from the dissection of animals when he said that these organs "ought to have" certain resemblances to those of man. Galen categorically used the word "have." However, not even in animals do the optic nerves have canals, nor are there communications between the third ventricle and the pharynx. Souques thinks that Galen, like Homer, nodded occasionally. Another of Galen's errors of fact was in the separation of motor and sensory nerves on the basis of their hardness, and still another, an egregious one, was the concept of the circulation of the brain. While the position of the arteries was well described, they were thought to contain only vital pneuma, and if blood oozed from their cut ends it was due to contamination through anastomoses with veins. Nothing indicates that Galen had any idea of the circulation of the blood. The epoch in these instances was stronger than the man.

As against the three or four major errors of Galen, his discoveries merit attention. The recurrent laryngeal nerves are described for the first time, and the separation of the ventral and dorsal roots, a discovery that required seventeen centuries to demonstrate definitely. Galen may have borrowed many an idea from his teachers and forerunners—their work exists but in fragments—but Galen built on it with his knowledge of vertebrate anatomy and physiology. "Galen founded experimental physiology. His magnificent experiments on the nervous system suffice to rank him with the princes of physiology. His great idea was to demonstrate that the brain is the center of voluntary movement and of sensibility, and he showed it beyond question. He proved that the spinal cord and the nerves drew from the brain, in effect, their sensory and motor faculties. By his transections of the spinal cord at different levels he produced quadriplegias, paraplegias and hemiplegias analogous to those of man, and he drew from these experiments the necessary applications to topographic localization of diseases of the spinal cord. His researches . . . on the mechanism of movement and of sensation have a direct bearing and may well stand comparison with modern investigation."

As a clinician, Galen fell below his level as an anatomist or a physiologist. While he clearly described focal convulsions and inaugurated psychotherapy, it was in localizing the diagnosis that he outshone the others of his time. In his writings, the gems of his own discovery were sandwiched in between thoughts on the ultimate causes of things, and between flights of rhetoric and philosophy that have no place in a treatise on anatomy. His explanations, while sometimes ingenious, were often foolish and sometimes puerile. Sometimes he even took refuge in the idea of Aristotle that Nature does nothing in vain. Add to this his polemics, and the reader must have patience to get to the heart of the matter.

Yet it was not as an anatomist or as a physiologist that Galen endured so long in medical authority, but as the founder of a system in medicine that was the counterpart of the system in natural history founded by Aristotle. That system of elements (air, water, fire, earth) was supplemented by the humoral system (blood, phlegm, bile, black bile) and the four primary qualities (dry, moist, hot, cold) and their various combinations. Health resulted from equilibrium among these, and disease from a break in this equilibrium. Galen's doctrine rested on errors of fact or of interpretation and on hypotheses, but it endured for fourteen centuries because physicians had lost the taste for scientific research. Even the succeeding political adversities served only to crystallize his doctrine among the Arabs, at Salerno, in the schools of the Middle Ages, where it was sufficient to translate and annotate Galen.

Galen fell when Vesalius showed that the pores did not exist in the interventricular septum of the heart. The demonstration of other errors followed, but it was long before it was generally admitted that Galen could have been mistaken. With the fall of his system, the wheat was lost with the chaff in the ruins.

"Today Galen has fallen into a deep—an unjust—disregard. His works are no longer read. Assuredly life is short and the domain of medicine immense. I should like, nevertheless, to recall this thought, borrowed from Galen, which Littré took as an epigram: Be familiar with the writings of the ancients. I know by experience that there is pleasure and profit in reading Galen. His neurologic work assures him an imperishable glory, and merits our particular gratitude. Able clinician, talented anatomist, physiologist of genius, he remains, I dare not say the greatest physician, since there is still Hippocrates, but at least the greatest neurologist of antiquity. I should add that we should also be thankful to him for having preserved the knowledge of his predecessors, and for having elevated medicine to the heights of a science and revealed the dignity of the physician."

FREEMAN, Washington, D. C.

OPHTHALMIC ASPECTS OF CEREBRAL SYNDROMES. JOHN N. EVANS, Arch. Ophth. **10**:241 (Aug.) 1933.

This paper is a review of the ophthalmologic literature correlating ophthalmology with various cerebral syndromes. Evans states that it is surprising how various studies group themselves to form complete pictures, and presents a schematic representation of symptomatology and the anatomic features. He calls attention to the fact that intracranial lesions occur as two types, expansile and nonexpansile. The material includes only such expansile lesions as intracranial hemorrhage, aneurysm, new growths, cysts, abscesses and granulomas. The symptoms and signs depend on local damage to the optic pathways or on direct or indirect damage through increased intracranial pressure. Local damage occurs through infiltration by inflammatory cells, disturbances of the blood and lymph supply, pressure erosion, direct and indirect compression of the expanding mass, localized action of toxins and invasion by neoplastic cells. From the point of view of the ophthalmologist local damage is recognized primarily through studies of the visual fields. By this means decrease in functional activity should be recognizable long before atrophy occurs and also before ophthalmoscopic or other ocular evidence is well established.

Atrophy of the optic nerve may involve the whole nerve or only some of the fibers. Atrophy affecting the nerve as a whole is most apt to originate in a nutritional disturbance (ultimately of the blood or lymph), in uniform compression with increased intracranial pressure (a questionable mechanism) or in massive action of toxins. The damage due to generalized intracranial pressure is manifested in atrophy of the optic nerve, choked disk and changes in the visual fields. Of the last, there are two distinct types; the first arises from increased intracranial pressure and the second from damage to the visual pathways by localized lesions. The types may occur together, and it is not always easy to differentiate one from the other. Alterations in the pupillary reflexes and the extra-ocular muscles also may indicate intracranial pressure.

Evans presents thirteen distinct syndromes.

1. Anterior Optic Pathway in Midline.—Outstanding characteristics are: (1) primary atrophy of the optic nerve of the same side; (2) swelling of the nerve on the side opposite the lesion and (3) anosmia. Later, direct pressure or erosion of the nerve as a whole would produce complete atrophy and the so-called concentric contraction and enlargement of the blind spot. In the final stages the whole field would be obliterated. Involvement of the adjacent structures as the damage progresses would give rise to such symptoms as (4) changes in personality and (5) weakness of the facial muscles and like signs.

2. Anterior Optic Pathway Not in Midline.—An expanding lesion arising in front of the chiasm and placed too far laterally to influence the olfactory nerves (e. g., growths of the sheaths of the optic nerve) gives rise to: (1) unilateral exophthalmos (apt to be painless) and (2) primary atrophy of the optic nerve of the same side. Whereas this type of disturbance is primarily orbital, its later stages give rise to symptoms originating within the skull. As the process extends backward, roentgenographic study discloses that (3) distortion of the optic foramen and (4) swelling of the optic nerve on the side of the exophthalmos follow, if the return flow of lymph and blood in the nerve is impaired. Finally, the growth may invade the cranial cavity sufficiently to give rise to increased intracranial pressure and then (5) swelling of the opposite nerve appears. Monocular exophthalmos can arise from a great variety of causes, such as hyperthyroidism, trichinosis, aneurysm and inflammation of the accessory sinuses of the nose. It is necessary to rule out these factors, but they seldom offer serious difficulties.

3. The Chiasmal Syndrome.—Characteristic findings are: (1) primary atrophy of the optic nerve, with (2) bitemporal defects of the visual fields and (3) a normal sella turcica, which, occurring in adult life, leads one to say that this is the purest form of the syndrome and probably due to a suprasellar meningioma. As the lesion progresses, secondary symptoms arise, such as: (4) increased intracranial pressure; (5) disturbances of the function of the pituitary gland; (6) absorption of the sella turcica, and (8) hydrocephalus.

4. Suprasellar Adenomas.—This is rather similar to syndromes 2 and 3. It is usually accompanied by enlargement of the pituitary fossa and mild symptoms of decreased function of the pituitary gland.

5. Craniopharyngiomas.—This again is similar to 3; the sella turcica is usually normal. Roentgenographic studies show suprasellar shadows of deposits of lime. In childhood they are accompanied by functional disturbance of the pituitary gland, and, with extension of the growth, there is increased intracranial pressure with a great variety of "neighborhood signs."

6. Disturbances of the Circle of Willis.—These are manifested by: (1) primary atrophy of the optic nerve; (2) bitemporal defects of the visual fields and (3) a normal sella turcica. Even so, diagnoses in these cases are made largely at autopsy.

7. Lesions Primarily of the Chiasm.—Here also the chiasmal syndrome of 3 is general. These cases are largely gliomas. The sella turcica shows a pear-shaped expansion. General neurofibromatosis is not uncommon.

8. Less Common Lesions.—The syndrome of bitemporal defects of the visual fields and a normal sella turcica applies here. Chordomas, which originate behind the chiasm, sooner or later affect the optic tracts. Certainly inflammatory processes, such as syphilis and those extending from the nasal accessory sinuses, may likewise give rise to the syndrome.

9. Pituitary Fossa.—Lesions arising in the pituitary fossa practically always originate in the pituitary body, pituitary adenoma being by far the most common disturbance. The basic symptoms are: (1) primary atrophy of the optic nerve; (2) half-field defects (this may be the upper or the lower portion of the field as well as the lateral portion) and (3) marked changes in the sella turcica. As already implied, symptoms of (4) hypopituitarism or of (5) hyperpituitarism occur, as the case may be. Enlargement of the lesions of the fossa below may force the chiasm upward against the circle of Willis, and under certain conditions a combination of symptoms may occur from the two lesions: the alterations in the pituitary gland and the disturbances in the blood vessels.

10. The Quadrigeminal Plate.—This syndrome is marked by: (1) the increased intracranial pressure syndrome (swelling of the nerve head, headache, vomiting, dulling of the intellect, contraction of the peripheral field and enlarged blind spots); (2) localizing signs of lesions of the quadrigeminal plate with disturbance of the extrinsic and intrinsic ocular muscles, cerebellar signs, disturbances of the skeletal muscles, indirect signs due to disturbances in more remote areas and vegetative dysfunctions (polyuria, maldevelopment and similar conditions).

11. Temporal Lobe (Temporosphenoid or Temporoparietal).—Disturbances of the temporal lobe may be expected with: (1) aphasia, when the lesion is on the left side; (2) homonymously placed defects in the visual fields which fluctuate; (3) a dreamy state; (4) the increased intracranial pressure syndrome and (5) symptoms of a systemic disturbance or symptoms from involvement of adjacent structures.

12. Parietal Lobe.—This syndrome comprises: (1) homonymous defects in the visual fields; (2) paresthesia; (3) anesthesia; (4) defects of muscle sense, with more or less (5) paralysis or spasticity of the muscles of the face, arm or leg. These symptoms may be associated with: (6) convulsive seizures and loss of consciousness and with the onset of (7) the increased intracranial pressure syndrome.

13. Occipital Lobe.—Involvement of the occipital lobe would be marked by: (1) homonymous defects of the visual fields; (2) the increased intracranial pressure syndrome and (3) visual hallucinations arising from (4) direct or indirect disturbances of the adjacent region of visual memory.

In concluding the review, Evans has quoted axioms which are important:

1. Repeated studies of the visual fields must be made if they are to have diagnostic value.

2. Sharply defined lesions are apt to produce sharply defined defects of classic shape in the visual fields.

3. Diffuse or infiltrating lesions produce atypical defects in the visual fields.

4. Conclusions as to the location of a lesion producing a particular defect in the visual field are based on the type of field, the shape of the field and the associated ocular and general symptoms.

5. Defects in the optic tract are differentiated from defects in the optic radiations by the presence of symptoms arising from an influence on the primary centers, possibly the hemianopic pupillary response to light, the use of the red-free filter to discover evidence of descending atrophy in the retinal nerve fibers, and the incongruity of the defects of the right and left visual fields (the more posterior the lesion, the more perfectly matched are the fields from the right and left eyes when superimposed).

Spaeth, Philadelphia.

RESULTS OF LUMBAR SYMPATHECTOMY IN THROMBO-ANGIITIS OBLITERANS. E. D. TELFORD and J. S. B. STOPFORD, Brit. M. J. **1**:173 (Feb. 4) 1933.

During a period of almost two years the authors performed about fifty operations on the autonomic nervous system by cervical-dorsal ganglionectomy or excision of the lumbar cords and ganglia. Of these cases, the first sixteen cases of thrombo-angiitis obliterans were selected for this study. All the patients studied were men whose average age was 47; three were Jewish, and all but two were engaged in sheltered work within doors. There was no basis for the contention that smoking is a causal factor. The Wassermann reaction was negative in all but one case. Routine observations on serum calcium and coagulation time yielded no results of interest. As for the duration of the disease, the longest history was twenty years, and in the shortest case symptoms developed which became crippling within the brief space of eight months.

With most patients the first complaint was intermittent claudication, with severe pain, rigidity or constriction about the calf of the leg. The more intelligent patients gave a history of initial coldness, usually in attacks, describing their feet at the time of the attack as "dead white." This suggests that in the early stage of the disease vasospasm is present. The cases were all bilateral, usually more pronounced in one leg than in the other. Seven patients made complaint of vascular disturbance in the hands, invariably of a spasmodic Raynaud type. In all cases the feet were very cold and the color was usually slightly dusky, though in some it was dead white. The dependent position produced some degree of rubor in nearly all cases, whilst elevation usually produced a distinct blanching. The dependent position, with cool air, gave the most comfort. In four cases no pulse could be felt below Poupart's ligament, while in twelve a strong pulse was present in the common femoral artery, but ceased abruptly about the division of the artery into the superficial femoral and deep femoral arteries. The point at which the pulse ceased is the point at which the sympathetic supply to the vessel has been shown to change from a perivascular plexus to a supply which is derived from the peripheral nerves.

Onychia is the commonest sign of impending grave trouble. Frequently, under a mistaken diagnosis, the nail is removed, whereon the nail-bed is transformed into an intractable, callous and painful ulcer, with no tendency to heal or to form a new nail. Four of these cases showed extensive gangrene in two or more toes.

In regard to the various methods of treatment, all have this in common: They have utterly failed to prove of any permanent benefit in treatment for this disease. This, of course, is exclusive of sympathectomy. Operative procedure in these cases consisted of removing on both sides a section of the lumbar sympathetic cord to include the second, third and fourth lumbar ganglia. The results were described as good in nine cases, meaning that the patient was free from pain and able to walk well. In three cases results were fair, indicating improvement as to pain and general condition, but little gain as to walking capacity. In four, results were unsuccessful in that there was no improvement or that subsequently amputation was necessary. Cases of onychia showed rapid healing following sympathectomy, but gangrene was little affected. The relief from pain is often complete and is the most striking and gratifying result of the operation. There are indications that this operation does arrest further progress of the disease.

There do not seem to be any untoward effects from such extensive removal of the lumbar sympathetic cord. In some cases movement of the bowels was more regular than before. No effects seemed to be produced in the pelvic organs. As for the muscular condition of the sympathectomized limbs, it was evident, when judged by ordinary clinical and functional tests, that they showed not the slightest difference from the normal.

FERGUSON, Niagara Falls.

A CLINICAL CONTRIBUTION TO THE STUDY OF FIBRILLARY CHOREA (PARAMYOCLONUS MULTIPLEX FIBRILLARIS OF KNY; MYOKYMIA OF SCHULTZE). M. GOPCEVICH and L. LOVISATO, Riv. di pat. nerv. **40**:545 (Nov.-Dec.) 1932.

The authors describe a case of paramyoclonus multiplex and review the literature concerning this rare condition, of which in the last forty years not more than

twenty cases have been published. Kny, in 1888, was the first to describe two cases of paramyoclonus multiplex fibrillaris; in 1895 Schultze described a case of the same nature which he called "myokymia." In analyzing their case, the authors ascribe the muscular contractions which they report to the expression of fascicular activity occurring uninterruptedly in more than one muscular fascicle, but without synchronisms. These contractions, though noticed by the patient, do not cause pain or visible movements of the limbs. In some cases the contractions are localized, while in others they are generalized. The contractions often spare the muscles of the neck and face. In the localized cases the myokymia may assume a paraplegic or monoplegic distribution.

Concerning the correlation of fibrillary chorea with the paramyoclonus of Friedreich, it was believed by Morvan that the former is merely a variety of the latter. The paramyoclonus may not differ from similar manifestations that accompany epilepsy in the so-called myoclonus epilepsy of Unverricht, of which the main features are the familial character and the association with epileptic seizures.

Sensory disturbances, from simple paresthesia to more definite neuralgia, may accompany the paramyoclonus. The deep reflexes are generally normal or exaggerated; occasionally they may be diminished or even abolished (Krebs). The electrical reactions generally disclose neuromuscular hyperexcitability to both faradic and galvanic stimuli. Generally speaking, motility is not interfered with by the clonic contractions. Rarely there is associated some muscular atrophy, as in a case described by Higier of atrophic myokymia of a paraplegic distribution associated with atrophy of the flexor group of the thigh. Few cases have been described in which there was muscular hypertrophy, as in the case of "myohypertrophia kymoparalytica" of Oppenheim. The duration of the disease is from three weeks to four months. Relapses occur. Chronic forms are observed occasionally, as in the case of Hoffman, of twenty years' duration, and of P. Bailey, of eight years' duration. Rarely the disease may have a stormy course and lead to death in a few weeks or months.

Pathogenetically, the cases may be divided into two groups: 1. The myokymia is symptomatic in the course of other neurologic conditions. 2. The muscular manifestations are more or less generalized, and the etiology is unknown. Some authors believed the condition to be the expression of a slight polyneuritis, and Biancone considered that the myokymia was the result of an exaggerated spinal reflex activity.

The question of the etiology of myokymia has been simplified by Bittorf, who thought that it was due to irritation of a peripheral neuron, which he included under the general heading of muscular cramps. The fact remains, however, that cramps are not as often observed as fibrillary contractions. According to the authors, fibrillary chorea is a neurologic syndrome of peripheral origin, the occurrence of which is conditioned by a physiopathologic mechanism, predominantly irritative, the cause of which is still unknown. FERRARO, New York.

THE BABCOCK DETERIORATION TEST IN STATE HOSPITAL PRACTICE. PHYLLIS WITTMAN, J. Abnorm. & Social Psychol. **28**:70 (April-June) 1933.

The Babcock deterioration test was given to 245 patients and to 26 nonpsychotic subjects at the Elgin State Hospital. This test assumes that remote memory remains relatively intact, since "words once learned are not easily forgotten" but remains as an indication of the mental ability the patient once had. The Terman vocabulary test is given to the patient to ascertain his original maximum intelligence. Since mentally deteriorated subjects have difficulty in making new associations and in retaining recent memories, twenty-four new tests are given to them. These twenty-four tests require the formation of new associations and the retention of recent memories. Both time and accuracy are taken into consideration, and a score is obtained which is termed the efficiency score. These twenty-four tests have been standardized, and each mental age can be immediately translated into a norm on this test scale. For example, a patient scores a mental age of 15 years

on the vocabulary test. The mental age of 15 years can be translated into a score on the twenty-four test scale, which is found to be 14.7. Let it be assumed, however, that a patient with dementia paralytica scored on the twenty-four test scale only 9.2. The difference between that which he should have scored and that which he did score (14.7 minus 9.2) leaves a difference of minus 5.5. This indicates the amount of mental deterioration the patient has undergone. A score below minus 3.5 is considered by the author to be significant of deterioration.

The 245 patients to whom this test was given were divided into diagnostic groups, and the average score of each group was enumerated as follows: the 98 cases of dementia paralytica scored minus 5.1; the 66 cases of alcoholism scored minus 2.3; the 26 cases of epilepsy scored minus 5.4; the 24 cases of schizophrenia scored minus 0.8; a group of 6 patients with manic-depressive psychosis scored minus 1.4; the 4 patients with organic disease of the brain scored minus 3.3; the 4 with psychoneurosis scored minus 0.6; the 4 with arteriosclerosis scored minus 4.9; the 14 cases in which the patients were not cooperative were given no score; the 26 nonpsychotic patients scored minus 1.2.

As a check on the reliability of the findings of the tests given to patients with dementia paralytica, both before and after malarial therapy was instituted, ward physicians who were familiar with the patients rated each patient according to the amount of improvement he was considered to have shown after therapy, without knowing the valuation of the deterioration scores obtained. In most cases there was a high degree of correlation between the standardized test rating and the psychiatrist's estimation of the patient—arrived at independently of the Babcock scoring. It was noted that the classes of mental disease that have the largest negative index are the psychoses in which mental deterioration is an important factor, namely, epilepsy, dementia paralytica, arteriosclerosis and alcoholism. The average indexes found for the so-called functional psychoses, schizophrenia and manic-depressive psychosis, agree with the general belief that there is no definite pathologic intellectual deterioration associated with these forms of mental disease. Seven cases classified as dementia praecox, paranoid type, in which the patients had been inmates of the hospital for five years or more, were tested to determine whether long-continued residence as patients within a hospital had caused a let-down in efficiency. No obvious mental deterioration was found. The deterioration test seemed to be a fairly reliable instrument for measuring the amount of improvement which takes place in a patient with dementia paralytica after fever therapy has been administered.

WISE, Howard, R. I.

PSYCHOSIS: ITS IMPORTANCE AS A PRESENTING SYMPTOM OF BRAIN TUMOR. LEO J. ADELSTEIN and MARTIN G. CARTER, Am. J. Psychiat. **12**:318 (Sept.) 1932.

Many patients with tumor of the brain are placed in hospitals for mental diseases because of the conspicuousness of the psychotic symptoms associated with them. Tumor of the brain, however, is not uncommon; it is found in from 0.5 to 2 per cent of general hospital autopsy material; in view of the frequency of associated mental symptoms, it must be kept in mind in the study of every psychotic patient. The authors cite seven cases of verified tumor of the brain accompanied by psychosis.

A man, aged 42, with attacks of violence, euphoria and threats to harm his family also suffered from headache, dizziness and convulsions. A left facial weakness and bilateral choked disk were found. Ventriculography showed marked foreshortening of the anterior horn of the right lateral ventricle. Operation disclosed a spongioblastoma in the right frontal lobe. A woman, aged 49, suffered from convulsions, visual hallucinations and delusions of persecution. The right pupil was larger than the left, and there was a bilateral Babinski sign. Roentgenograms showed thinning of the posterior clinoids. Necropsy revealed a spongioblastoma in the anterior portion of the corpus callosum. A woman, aged 44, had complained of headaches ever since she had sustained a cerebral con-

cussion in an accident six years prior to admission. At this stage she had become blind, but in visual hallucinations "saw" a group of Chinamen at her bedside. On examination, bilateral Babinski sign and bilateral optic atrophy were found. Autopsy disclosed an astrocytoma at the vermis of the cerebellum. A woman, aged 56, had headache, vertigo, weakness, difficulty in speaking and visual hallucinations. The disks were choked. She fell backward and to the right when tested. The hallucination was constant, and consisted of an impression that three masked soldiers were at her bedside. Bárány tests showed reduced responses. Ventriculography disclosed a marked internal hydrocephalus, with bulging of the floor of the posterior horn of the right lateral ventricle. At operation an astrocytoma of the right cerebellar lobe was removed. A woman, aged 56, had had an operation for removal of a lipoma of the neck, following which there developed headache and visual hallucinations not unlike those of delirium tremens. Anosmia and choked disks were found on both sides. There was a left facial weakness. Autopsy disclosed a spongioblastoma of the splenium of the corpus callosum. A woman who exhibited characteristic "Witzelsucht" and an anomial aphasia had ataxia and hemiparesis on the right. Autopsy revealed multiple meningiomas, one arising from the falx at the left frontal area, one from the longitudinal sinus in the right parietal region, one at the tentorium and one in the left occipital region. The last patient, a white woman, aged 35, was restless, irritable and irrational; she complained of headache, vomiting and double vision. Choked disk was bilateral; exophthalmos was noted on the right, while the left arm and leg were spastic. A right temporal ganglioneuroma was found at autopsy.

From an analysis of the psychotic symptoms in these cases the authors are unable to postulate any localizing value to purely mental symptoms. Localization must depend largely on roentgenologic and neurologic findings.

DAVIDSON, Newark, N. J.

NEURALGIA OF THE GLOSSOPHARYNGEAL NERVE. J. TERRACOL, Rev. d'oto-neuro-opht. **11**:161 (March) 1933.

Several months after hysterectomy for an ovarian cyst, a woman, aged 46, suffered with crises of pain in the lateral pharyngeal wall and the left ear. The crises increased in intensity and frequency and were accompanied by tinnitus, temporary decrease of acuity of hearing, occipital headache, pain on pressure over the exit of Arnold's nerve, exaggeration of the pharyngeal reflex and lowering of the right palatine arch. Nothing significant was discovered in the several examinations made, except that roentgenography disclosed an osteo-arthritis of the cervical spine. Rapid recovery followed appropriate therapy, chiefly diathermy.

The posterior cervical sympathetic syndrome was studied by Barré and Leiou. There are three clinical forms, depending on the three different localizations: (1) the superior cervical syndrome (true posterior cervical sympathetic syndrome); (2) the middle, which is characterized by paresthesias, glossodynia, difficulties in swallowing, muscular atrophy of the pharynx and laryngeal disturbances, and (3) the inferior syndrome, represented by painful amyotrophic and paralytic phenomena in the domain of the superior brachial plexus. The three forms merge into each other clinically and have a common anatomicopathologic basis: osteo-arthritis of the cervical column. Most often the osteo-arthritic process involves the region of the spinal foramina. Terracol thinks that this process is the result of a broken physicochemical equilibrium in the colloids constituting the interstitial plasma. This equilibrium is the product of three principal factors: sanguine (composition and quality of the blood); circulatory (more or less rapid exchanges in the territory under consideration) and mechanical (pressure, traction and tangential movements). Most of the patients are demineralized, the trouble often appearing in women at the menopause or after castration. When there is loss of calcium, the blood takes its needed supply from the osseous system. The circulatory factor is most important. All the phenomena of ossification are ruled by the circulatory factor. The nutritional arteries of the cervical column are the dorso-

spinal branches, coming chiefly from the vertebral artery. No other important artery has so long an intra-osseous course. All osteo-arthropathies are the result of disturbed vasomotor innervation. The periarterial sympathetic seems to be the sole trophic nerve, and trophic phenomena must be considered as circulatory phenomena. Vasomotor disorders explain the symptoms and pathogeny of the troubles observed. Narrowing of the spinal foramina is not a sufficient explanation. This disorder may be determined by disturbance of the vertebral nerve, which is the vasomotor organ of the vertebral artery. In the case reported the tinnitus and diminished hearing may be explained by a vasomotor disturbance of the vertebral artery, but the neuralgia must be attributed to the glossopharyngeal nerve. There is, therefore, an association of neuralgic and sympatheticalgic phenomena, easily explained by the frequent anastomoses of medullated and nonmedullated fibers.

DENNIS, Colorado Springs, Colo.

INTERPRETATION OF REFRACTIVE CONDITIONS IN THE PERIPHERAL FIELD OF VISION. C. E. FERREE and G. RAND, Arch. Ophth. **9**:925 (June) 1933.

This article reports further study and is a continuation of the authors' paper, "Refraction for the Peripheral Field of Vision" which appeared in the May, 1931, issue of the *Archives of Ophthalmology*, p. 717, and was reviewed. It was the authors' purpose to make a more comprehensive analysis of their findings in studying the refractive situation from the center of the eye to its periphery. Some of their findings, in concluding their work, follow. They present them only as incentives for a wider study of the refractive situation of the eye as projected in the peripheral portions of the field.

The relation which the refractive conditions in the peripheral field sustain to acuity in the peripheral field, to achromatic and chromatic sensitivity in peripheral vision and the limits of the form and color field, and to the anomalies and irregularities in peripheral perception of space is important. In this connection it may be noted that the conditions for the formation of an image are so bad for objects in the peripheral field that one can only marvel that peripheral vision is as good as it is, and that the peripheral portions of the retina should have attained as high a development as they have.

The study has as its aim the ability to detect and determine the amount of refractive asymmetry lying in the ocular structure representing the two halves of the field of vision, and the possibility of determining, within rather wide limits in cases of refractive asymmetry, whether the defect is in the refracting system and its placement in relation to the axis of vision, or in the conformation of the retina or shape of the eyeball, or in both. The possible bearing of asymmetrical refraction in the peripheral field may give an explanation of cases in which central vision cannot be substantially improved by correction in eyes which show no central scotoma. Asymmetrical refraction may play a rôle in cases of ocular deviation, and the demonstration of such a condition may have a bearing on the treatment.

The possibility is present of determining roughly the conformation of the retina and the shape of the posterior half of the eyeball by refracting the eye for the peripheral field, of obtaining information as to the comparative length of the eyeball and the strength of the refracting system in both emmetropic and ametropic eyes, and last, of estimating with a fair degree of certainty the relative importance of the length of the eyeball and the strength of the refracting system as causal factors in the refractive defect in hyperopic and myopic eyes.

SPAETH, Philadelphia.

CHANGES IN THE BRAIN IN CARDIAC DISEASES. G. BODECHTEL, Ztschr. f. d. ges. Neurol. u. Psychiat. **140**:657 (July) 1932.

Apart from the changes in the brain caused by emboli, little has been written on the findings in the nervous system in heart disease. Flater found cerebral symptoms in 50 per cent of cases of ulcerative valvular disease. Much credence

has been given to a toxic factor in the nonembolic cases, but Bodechtel minimizes this theory. He believes that the diffuse cerebral changes in such cases are due to vascular spasms, a factor which has not been generally recognized until recent years. He believes further that in cases of embolism the embolic abscesses are formed first by a softening that is the result of a vessel spasm, in which bacteria coursing in the blood stream settle as in a locus minoris resistentiae.

Of two cases of congenital heart disease, one showed numerous areas of necrosis in the white matter, especially in the occipital region, with accumulations of gitter cells in many places. The other case showed slight cortical changes, with perivascular hemorrhages around apparently intact vessels. Most of the changes were in the white matter, which showed glial accumulations of gitter cells and astrocytes, usually in the region of vessels. Small necroses were found as well. In histologic preparations there were scattered patches of loss of myelin with pathologic axis-cylinders, and deposits of fat. Among other things, this case shows that perivascular hemorrhages may occur in heart disease as well in numerous toxic disorders.

Bodechtel studied the brains in thirty-eight cases of heart disease in adults with cardiac insufficiency, with old or recent endocarditis. Of the thirty-eight cases, nine showed only changes in the cells in the brain without grosser changes; six showed significant loss of cells; thirteen showed pallor or softening in the cortex; seven were without significant changes, and three showed "embolic encephalitis." There is no specific type of cerebral disease of the cells in cardiac disorders. Bodechtel found acute cell disease, ischemic cell disorders and chronic cell changes, among other types. Various types of cortical changes were observed: scattered loss of cells, focal areas of necrosis, areas of recent glial reaction, areas of recent softening or colliquation necrosis and focal loss of cells.

Bodechtel found cortical and striatal areas in cases of Sydenham's chorea, with loss of cells due, he believed, to vascular involvement. These areas are not characteristic of all cases of chorea, but they may occur at any time.

ALPERS, Philadelphia.

SYPHILIS OF THE CEREBELLO-PONTINE ANGLE. E. D. FRIEDMAN, SAMUEL BROCK and PETER G. DENKER, Am. J. Syph. **17**:330 (July) 1933.

Syphilis, although widely disseminated within the central nervous system, seldom is associated with cerebellopontile angle syndromes. During a ten year period the authors observed five instances of syphilis of the cerebellopontile angle; one, in a girl, aged 10, was due to congenital disease; the other patients were adults in the fourth decade. The onset was sudden in three cases and gradual in two. One patient complained of headache, vertigo and progressive deafness in the right ear; he had a right facial paresis, a Romberg sign, with sway to the right, and awkwardness in the right arm; and the right labyrinth showed no response to caloric tests. The Wassermann reaction of the blood was two plus, and of the spinal fluid, one plus, and the colloidal gold curve was 3333211000. Antisyphilitic therapy relieved the headache, but did not reduce the deafness. The same symptoms and clinical findings were reported in another case; in this patient, however, the Wassermann reaction was four plus with both blood and spinal fluid, and there was an even more syphilitic type of gold curve. Treatment was entirely unsuccessful. The third patient had irregular pupils, horizontal nystagmus to the right, diminished left corneal reflex, left facial hypesthesia, left peripheral facial paresis, past pointing to the left and partial nerve deafness on that side. Labyrinthine irritability was completely lost in the left ear. The Wassermann reaction, both with the blood and with the spinal fluid, was four plus. Moderate improvement followed treatment. The fourth patient was the only one with papilledema. The findings otherwise were the same as in the third case. Treatment in this instance, however, was more successful. The last patient—a girl with congenital syphilis—had bilateral deafness, with facial weakness, nystagmus, adiadokokinesis and facial hypesthesia, all on the left side. The Wassermann reac-

tion with the spinal fluid was negative, but with the blood, in both the patient and her mother, was four plus.

The authors stress the frequency of involvement of the fifth nerve and the normal condition of the optic disks (in four of the five cases), the absence of coarse nystagmus, the cerebellar signs and the facial weakness. The latter, unusual in early cases of cerebellopontile angle tumor, is almost a presenting sign in syphilis of this area.

DAVIDSON, Newark, N. J.

THE PROBLEM OF TRAUMATIC PARKINSONISM (A CONTRIBUTION TO THE KNOWLEDGE OF EXTRAPYRAMIDAL MOTOR DISTURBANCES FOLLOWING BRAIN INJURIES). W. HEYDE, Arch. f. Psychiat. **97**:600 (Sept.) 1932.

Heyde introduces the subject with a discussion of the present day concept of the rôle played by trauma in the production of parkinsonism. Reports in the literature vary greatly, some authors taking the stand that trauma is at most to be regarded only as a precipitating factor, never as a primary one, while others are of the opinion that traumatic lesions may be totally responsible for the development of the typical syndrome. He finds that one of the reasons for such a variation in opinions is the fact that authors vary in their definitions of the disease process. Heyde differentiates between paralysis agitans with all the symptoms characterizing it, on the one hand, and Parkinson-like symptom complexes that show a number of other signs in addition to the circumscribed syndrome.

He reports twenty-eight cases of this syndrome out of a total of 683 cases of definite injuries of the skull and brain. Detailed study of the past history of the patients as well as the clinical pictures found after the accident leads Heyde to the conclusion that in no single case of the group could he find a definite set of factors that would prove a distinct relationship between the disease process and the accident. In nine cases the previous history contained attacks of encephalitis preceding the accident; the parkinsonian syndrome was most probably based on a postencephalitic condition. In three cases there were so many symptoms that did not belong to the parkinsonian syndrome that a diagnosis of paralysis agitans should not have been made. In the remainder of the cases no direct relationship could be established between the development of the disease and the accident. Hereditary trends, the age of the patient, the condition of the blood vessels and a number of other factors made it appear possible that some other causes were to be regarded as just as basic in the development of the disease as the trauma itself. The author thinks that although his material does not altogether exclude the possibility of a traumatic parkinsonism, nevertheless none of the cases is sufficiently clear to prove that such a relationship can be established.

MALAMUD, Iowa City.

STUDIES IN THE BLOOD VOLUME OF EPILEPTICS. MORGAN B. HODSKINS, RILEY H. GUTHRIE and JAMES Z. NAURISON, Am. J. Psychiat. **11**:623 (Jan.) 1932.

Within recent years seven methods for the treatment of epilepsy have been presented and reported as successful. These are: dehydration, starvation, enforcement of ketogenic diet, administration of calcium or ammonium salts, intravenous injection of hypertonic solutions, colectomy and fever induction. The success that has attended starvation cannot be due to acidosis, for it is precisely in certain conditions of ketosis, such as diabetic coma, that convulsions occur. It is more likely that reduction of the fluid volume in the body suppresses the seizures. The same is true of the ketogenic diet which by removing surplus sodium reduces body fluid. The dehydration value of the calcium and ammonium salts, as well as of intravenous injections of hypertonic solutions, is well known. Colectomy, when successful, appears to owe its success to the removal of the fluid-absorbing bed of the alimentary canal with subsequent watery diarrhea and fluid discharge. The association of dehydration with fever is well understood. It would appear, there-

fore, that these diverse and frequently successful technics for controlling convulsions have in common the single factor of dehydration.

It is also to be noted that there are three diseases in which the incidence of epilepsy is remarkably low. These are Buerger's disease, hypothyroidism and diabetes. In all of these, a low blood volume has been found. It is the purpose of the investigations of the authors to determine the blood volume in epileptic patients. Seventy-eight patients, all subject to epileptic seizures, were examined when not under treatment, in intervals between attacks; an average of 83.2 cc. of blood volume per kilogram was found. In a normal control group the average was 77. Nine of the epileptic patients examined during fits showed a blood volume of only 72.5 cc. per kilogram.

Efforts to reduce blood volume by ammonium nitrate therapy were unsuccessful, and the failure to alter the blood and plasma volumes and plasma carbon dioxide was accompanied by a failure to reduce the number of convulsions. The authors conclude that epileptic patients tend to have a blood volume higher than normal persons, and that the convulsive attack is accompanied by a sudden disturbance in cerebral vasomotor control.

DAVIDSON, Newark, N. J.

THE HISTOPATHOLOGY OF EXPERIMENTAL INSULIN INTOXICATION. A. STIEF and L. TOKAY, Ztschr. f. d. ges. Neurol. u. Psychiat. **139**:434 (April) 1932.

Insulin intoxication was produced in four rabbits and four dogs. In the former the period of intoxication lasted from eight to ten weeks, and the clinical symptoms were few. They were more pronounced in the dogs and consisted of sialorrhea, perspiration, tremors, spasms, epileptiform attacks and catatonic and cataleptic postures. Grossly, the brains showed no abnormalities except extreme dryness and a tendency to break. The histologic findings were similar in rabbits and dogs. In general the nerve cells showed the severe changes of Nissl, with areas of sclerotic nerve cells and cells with acute and chronic changes. The glia took little part in the process, but in some places there was a reaction of the oligodendroglia and microglia. There were areas in which a marked mesodermal proliferation had taken place, with an increase in the number of capillaries. While the changes were diffuse, there were also focal changes. There were cortical areas in which the upper cortical layers were destroyed, others in which the lower layers were gone, and still others in which complete sectors had disappeared. In the rabbit the temporal lobes were most severely involved. In the basal ganglia the putamen and caudate were severely involved, while the pallidum showed but slight changes. The nuclei supra-opticus and paraventricularis were severely involved. The vessels were hyperemic everywhere, especially in the hypophysis. There were small hemorrhages in the infundibulum.

The changes in these cases are not specific. They are present in other intoxications, such as morphinism and uremia. There is a certain resemblance to the changes occurring in lead and guanidine intoxications. Besides the general intoxication, circulatory disorders play a rôle, as indicated by the lamellar degenerations in the cortex. Such disturbances have been postulated in man because of the presence of symptoms such as aphasia and hemiplegia. Redisch was able to observe with the capillary microscope arterial spasm and dilatation in cases of hypoglycemia. Some investigators believe that the changes in the brain are the direct result of the insulin; others attribute them to the hypoglycemia.

ALPERS, Philadelphia.

EXPERIMENTAL MERCURIAL POISONING OF RABBITS. A. E. KULKOW, D. S. FUTER and M. E. TORNOPOLSKAJA, Arch. f. Psychiat. **96**:661 (May) 1932.

Eight rabbits were subjected to the effects of mercury vapor in a specially constructed cage for two or three hours daily for from five weeks to four months. Death occurred spontaneously in all but one animal. In seven, autopsies were performed and histopathologic studies were made. 1. Clinical Changes: In all the animals there were generalized weakness, increased salivation and tremors of

the body and extremities. The time of onset of the symptoms varied from several days to one month. Toward the end there were paralyses and sphincter disturbances. There was loss of weight; the blood showed an increase of hemoglobin, mild leukocytosis and granulations of the red blood cells. There was a gradually developing acidosis in the blood and cerebrospinal fluid, with hypoglycemia and a decrease in the body temperature. There was also a deposit of calcium in various organs of the body, with signs of nephritis.

2. Anatomic Changes: There were changes in the ganglion cells, the blood vessels and the Hortega cells. The ganglion cells showed lysis and vacuolation, which were particularly pronounced in the dentate nucleus and cornu ammonis. The neuroglia was increased and the Nissl bodies were diminished. In some animals there were acute swelling of the cells, especially of the trigeminus nucleus, and disturbances in the cerebellum. There was also lipoid degeneration in the ganglion cells. The blood vessels of the cerebrum showed congestion and dilatation, with punctate hemorrhages. In some animals there was lymphocytic infiltration around the blood vessels. The Hortega cells showed degenerative changes, with thickening of the processes and development of gitter cells. The most interesting finding in the brain was the occurrence of encephalitic-like foci which could not be well distinguished from the inflammatory processes. Of the other organs of the body, those most affected were the liver, the lungs and the kidneys.

MALAMUD, Iowa City.

THE BIOCHEMICAL SYNDROME OF UREMIA. GEOFFREY THOMPSON, Brit. M. J. **2**:1134 (Dec. 24) 1932.

The case is reported of a healthy young man who was kicked in the left loin while playing football. Severe hematuria followed. The kidney was explored and was found to be hopelessly ruptured, necessitating its removal. The patient lived for ten days after the operation without secreting a drop of urine and then died of uremia. Cystoscopy, confirmed by postmortem examination, showed that he was the subject of congenital absence of the right kidney and ureter. In this case the temperature rose to 101 F. after the operation but gradually became lower, and for the last four days steadily remained subnormal (97 F.). The pulse rate rose to 140 after operation, but fell and remained steadily between 90 and 110 until death. The blood pressure did not rise beyond the normal limits. There was no hypertension, but a marked fall in the diastolic pressure. On the fifth day following operation, definite uremic symptoms appeared, when he became drowsy and a frontal headache developed. The nonprotein nitrogen of the blood rose rapidly to over 200 mg. per hundred cubic centimeters in five days. The condition bordered on coma, but when aroused the patient could speak intelligently and complained only of headache. A peculiar generalized fibrillary twitching of all the somatic muscles developed. There was also perpetual vomiting. At no time was there the slightest trace of edema anywhere. In spite of marked acidosis, there was no air hunger or hyperpnea. There was no stomatitis, diarrhea or excessive thirst.

This case is presented as an example of pure and uncomplicated uremia. The convulsive phenomena usually associated with uremia were absent. Toxic features were marked. Hypertension was absent. The author makes a plea for a more clearly fixed definition of the term uremia. FERGUSON, Niagara Falls, N. Y.

CERTAIN DISORDERS OF THE OPTIC NERVE OF ORBITAL, NASAL AND GENERAL TOXIC ORIGIN. C. PASCHEFF, Ann. d.ocul. **169**:835 (Oct.) 1932.

Among disorders of the optic nerve that arise from orbital causes, Pascheff speaks especially of two types: (a) papilledema caused by compression of the retinal vessels immediately posterior to the eyeball in a case of echinococcus cyst of the orbit; after extirpation of the echinococcus central vision and vision in the peripheral field are reestablished quickly; (b) atrophy of the optic nerve

following compression of the nerve in the optic canal in a case of oxycephaly associated with congenital syphilis; necropsy revealed: narrowing of the anterior cerebral fossa, the orbits and the optic canals; strong digital impressions in the skull, and numerous osseous ridges and pointed exostoses in the interior; a deep middle cranial fossa with numerous depressions in the bones; changes in the sella turcica and the diameter of the skull.

Among rhinogenic disorders of the optic nerve, Pascheff calls attention to the uncertainty in diagnosis and treatment. He describes: (a) Slight monocular edema of the optic nerve with blindness in two cases. The blindness disappeared completely in one case after the continuous application of epinephrine to the nasal mucous membranes; in the other a paracentral scotoma persisted which included the blind spot. (b) Acute neuritis, which disappeared after ethmoidectomy leaving a paracentral scotoma that included the blind spot. As disorders of the optic nerve following an acute general intoxication, Pascheff presents two cases of complete blindness in which vision was reestablished. In one, improvement occurred in central vision and in the other, in peripheral vision. An absolute central scotoma was present in one case and in the other, concentric contraction of the visual field.

BERENS, New York.

SPONDYLOLISTHESIS. H. W. MEYERDING. Surg., Gynec. & Obst. **54**:371 (Feb. No. 2A) 1932.

Meyerding is convinced that spondylolisthesis is more common than has previously been supposed. The disorder is a subluxation of lumbar vertebrae, generally the fifth, and occurs most commonly in farmers, housewives, laborers and others engaged in active physical work. Among the etiologic agencies are occupational strain, pregnancy, obesity and trauma. In most instances, Meyerding thinks, a congenital defect in lumbosacral architecture underlies the tendency to subluxation. Practically all the patients complain of backache, often with pain in the hips or lower extremities. Weakness, numbness, stiffness of the spine and a sense of relief in the recumbent position are additional symptoms. Among the physical signs are prominence of the sacrum, with a depression just above it, muscular spasm, short torso, broad pelvis, prominent erector spinae masses and roentgenologic findings. Anteroposterior roentgenograms reveal a shortening of the lumbar portion of the spinal column and show the imposition of the fifth lumbar vertebra on the sacrum, with a conspicuous "cocking up" of the spinous process. Lateral roentgenograms are even more valuable; they disclose the degree of subluxation, the condition of the neural arch, the shape and size of the involved vertebrae and the angulation of the lumbosacral joint. Treatment requires traction, immobilization and recumbency. For patients who must work, fusion operations are indicated—ankylosis of the lower vertebrae of the lumbar portion with the upper part of the sacrum being recommended by Meyerding. Neurologic signs are usually absent, although paresthesias over the saddle area occur in some cases.

DAVIDSON, Newark, N. J.

OBSERVATIONS ON THE HAEMATOPOIETIC HORMONE IN PERNICIOUS ANEMIA. ROGER S. MORRIS, LEON SCHIFF, JOHN H. FOULGER, MURRAY L. RICH and JAMES E. SHERMAN, Brit. M. J. **2**:1050 (Dec. 10) 1932.

The authors found that normal human gastric juice, unconcentrated, was practically inert, and that this juice concentrated by evaporation and injected intramuscularly showed slight activity. When, however, concentration was carried out by distillation in vacuo, a highly potent material was obtained, as indicated by reticulocyte response and by maturation of red blood corpuscles. It is destroyed by boiling, is dialyzable through collodion, and is exhaustible. It withstands chemical treatment which is known to destroy enzymes. It is therefore probably a hormone. Its presence was demonstrated in the gastric juice of swine, dogs and cattle.

The case history is reported of a man suffering from pernicious anemia, who was given 4 cc. of a fraction representing 3 liters of swine juice. The following day the reticulocytes rose to 4.4 per cent as opposed to from 0.6 to 1.3 per cent previously. Four days after injection they were up to 28.8 per cent, and six days after to 39.3 per cent. A maximum reticulocytosis of 42.9 per cent was reached ten days after injection. Within a week following the injection there was remarkable subjective improvement. At the end of two weeks, increase in the number of red cells and percentage of hemoglobin was first noted. Thereafter there was a steady rise in both until about three months later, when examination of the blood showed 4.5 million red cells and hemoglobin 93 per cent. The patient had received no further treatment after the original injection.

FERGUSON, Niagara Falls, N. Y.

ACUTE PURULENT FRONTAL SINUSITIS WITH OCULO-ORBITAL COMPLICATION: CEREBELLAR AND LABYRINTHINE PHENOMENA; OPENING OF BOTH FRONTAL SINUSES AND EXPLORATION OF THE RIGHT FRONTAL LOBE OF THE BRAIN; FIXATION ABSCESS; CURE. CANUYT, LACROIX and SCHEPENS, Rev. d'oto-neuro-opht. **10**:735 (Dec.) 1932.

A young girl, with an acute exacerbation of chronic frontal sinusitis on the right side but with no cerebellar or labyrinthine signs, was operated on, and external drainage was instituted. One week later heaviness of the head, vertigo and vomiting appeared, and the patient was unable to stand. Lumbar puncture relieved the symptoms temporarily and revealed a normal fluid, except that the pressure was slightly increased. Neurologic examination revealed prostration, a tendency to fall backward, an incorrect result in the heel-to-knee test, a bilateral Kernig sign, slight stiffness of the neck, vertigo, nystagmus to the left in all positions of the eyes, incontinence and difficulties of speech. Nineteen days after the original operation the left frontal sinus was opened, and the right frontal lobe was explored, with negative findings. A fixation abscess (aseptic abscess) was produced and opened five days later. Immediate improvement began, and recovery was rapid. There is no consensus as to the operative treatment in cases of acute suppuration of the frontal sinus with orbital complications. The authors believe that the sinus should be opened promptly and widely, with external drainage and without curetting the sinus walls or the nasofrontal duct. The curative action of fixation abscess in grave septic conditions is extolled.

DENNIS, Colorado Springs, Colo.

A CASE OF SPONTANEOUS NYSTAGMUS DIRECTED ALTERNATELY TO THE RIGHT AND TO THE LEFT. BUYS, J. de neurol. et de psychiat. **32**:715 (Oct.) 1932.

The author reports the case of a patient, aged 49, who had diminished vision and dizziness, which was spontaneous or induced by abrupt movements. This was accompanied by slight nausea. The general health of the patient was not good. He had had malaria and a condition associated with hematuria. He had two children, both of whom were well. There was a nystagmus which was directed alternately to the right and to the left in periods of from one to two minutes, which were separated from the following period by an interval of five seconds. It was not associated with the pulse nor modified by sudden movements or positions of the head. The attacks began first with a slight movement, which progressed to great intensity and then diminished to entire disappearance. During the rest period, lateral rotation of the eyes would induce a nystagmus. In the Romberg test the patient tended to fall to the side away from the nystagmus, and in walking with the eyes closed, he tended to fall away from the nystagmus. There was an apparent deafness on the left. There were no changes in the reflexes, nor in sensation; there was no ataxia; the Wassermann test was weakly positive. Buys believes that only two similar cases have been reported. He states that if the centers for nystagmus are antagonistic and constantly stimulated, one after the

other, on occasion, by habitual movements, and if one concedes that tone is modified for exchanges of energy, it is not impossible to admit that the alternation might be the result of permanent excitation. The only possible source of excitation is that which is the result of an old otitis. WAGGONER, Ann Arbor, Mich.

PSEUDOHYPERTROPHIC MUSCULAR DYSTROPHY OCCURRING WITH SYPHILIS. F. G. LINDEMULDER, Am. J. Syph. **16**:86 (Jan.) 1932.

Pseudohypertrophic muscular dystrophy is rarely seen in association with neurosyphilis, and to the meager literature on the subject Lindemulder adds this report of a case. A man, aged 26, whose chief complaint was weakness, had had a chancre at the age of 18 and had received no treatment for it. Three years later, he first noticed weakness and loss of weight; atrophy of the arms and legs rapidly followed, the calf and forearm muscles enlarging in the course of the illness. At the age of 26, eight years after exposure to syphilis and five years after the onset of symptoms, he had a waddling gait, lordosis, atrophy of the shoulder girdle and arms, pseudohypertrophy of the calf, anisocoria, absent abdominal and patellar reflexes, negative electrical reactions and normal sensory findings. Objectively, the case was typical of pseudohypertrophic muscular dystrophy, except for the pupillary reflex findings. The spinal fluid was of normal pressure but contained 180 cells per cubic millimeter; the reaction to the Kahn test was 4 plus both in the blood and in the spinal fluid. The gold curve was 1,112,321,000. The patient received mercury both intramuscularly and by inunction, and potassium iodide by mouth. At the end of two months he had gained 9 pounds (4.1 Kg.) and believed that he was stronger. His gait had improved. As to the etiologic relationship between the syphilis and the dystrophy and the effects of antisyphilitic therapy, Lindemulder's conclusions are indeterminate. DAVIDSON, Newark, N. J.

INTRACRANIAL AND SPINAL METASTASES IN GLIOMAS OF THE BRAIN. HUGH CAIRNS and DOROTHY S. RUSSELL, Brain **54**:377 (Dec.) 1931.

In eight of twenty-two consecutive full necropsies in cases of glioma spinal metastases were observed, thus showing a much higher frequency of this process than has hitherto been suspected. Spinal or cerebral metastases may be found in medulloblastomas, neuro-epitheliomas of the retina, glioblastoma multiforme, astrocytoma and ependymoma. The extent of metastases varies approximately with the malignancy of the primary tumor; they appear to spread as much by direct extension as by metastasis. The metastases from glioma seem to be limited to the central nervous system and to be disseminated by the cerebrospinal fluid.

Spinal metastases appear to arise by implantation along the subarachnoid space. An important fact is the accessibility to the ventricular system or basal cisterns. By studying the cytology of the secondary deposits in the subarachnoid space, where the tumor cells may grow on a free surface, much may be learned of the nature of the primary growth. Increase of protein in the spinal fluid in cases of intracranial tumor does not necessarily indicate the presence of spinal metastases. When this is encountered in children it should probably be regarded as suggestive of spinal metastases. Operation is not necessarily contraindicated when metastases are found, but in the presence of extensive metastases malignant gliomas are not suitable for operation. MICHAELS, Boston.

THE ORIGIN OF TUMORS. J. P. LOCKHART-MUMMERY, Brit. M. J. **1**:785 (April 30) 1932.

In this paper the author begins by remarking that the secret of tumor formation lies somewhere in the study of the normal tissue cells and not in the study of tumor tissue. He then briefly enumerates the properties of tumors and attempts to show that his theory of tumor production will explain their etiology.

He emphasizes the fact that the essential difference between a normal cell and a tumor cell is one of behavior and not of apparent structure. Tumor cells are normal cells which are behaving abnormally. The chief controlling mechanism of the cell resides in the nucleus. All cells, both germ and somatic, breed true to their parent cells, and this breeding is controlled by the genes in the nucleus. Therefore, when changes or mutation of the genes occur the daughter cells will always breed true to the mutation. Thus Lockhart-Mummery sees tumors as a result of mutation of the genes controlling the division of somatic cells. The cells in the mutated colony or the tumor will be normal cells, except that their rate of production will be faster. For the time being this theory does not offer any possible solution for the prevention or cure of tumors. On the other hand, it is well known that when a cause of disease is established one is in a fair way to discovering how to prevent and to cure it.

FERGUSON, Niagara Falls, N. Y.

CHRONIC SUBDURAL HEMATOMA: A STUDY OF EIGHT CASES WITH SPECIAL REFERENCE TO THE STATE OF THE PUPIL. ABRAHAM KAPLAN, Brain **54**:430 (Dec.) 1931.

The ages of the patients in the group reported varied from 23 to 66 years (average 43); there were six male and two female patients; the lesion was unilateral in seven cases and bilateral in one. The lucid interval presented the symptoms of headache, drowsiness and vomiting. The spinal fluid was bloody in only two cases. In five cases a dilated pupil was found on the affected side, and in one case palsy of the third nerve was observed on the side corresponding with the lesion. In seven of the eight cases there had been a definite injury of the head. From a review of previous studies it is suggested that chronic subdural hematoma is a result of trauma to the head, displacing the brain with a resulting tear of one or more cerebral veins. In 50 per cent of the cases the hematoma contains liquefied material having the appearance of blood-stained serum. The importance of observing the pupillary action and misleading pyramidal tract signs are discussed. A history of mild trauma, followed after a latent interval of several days, weeks or months by headache, vomiting and drowsiness, should make one suspicious of a subdural hematoma. The treatment is operative and may follow an exploratory trephination over the temporoparietal region on the side showing a dilated pupil.

MICHAELS, Boston.

PERSONALITY AND CATATONIC DEMENTIA PRAECOX. JOSEPH R. BLALOCK, Psychiat. Quart. **6**:625 (Oct.) 1932.

Blalock studied the personalities of twenty-five men suffering from catatonic dementia praecox and free from physical disease. The Hoch-Amsden technic for studying personality, as modified by Kirby, was used. Nine of the patients were definitely introverted, and one was definitely extroverted; the remaining fifteen were well balanced in this field. There was nothing striking in the analysis of the traits, as to knowledge, intelligence or judgment. The majority were awkward in the use of tools. The output of energy was definitely but not markedly reduced. Three fourths of the patients had always been bashful, and two thirds of them were stubborn, aloof, sensitive and devoid of extensive external interests. Nearly all of them were overconscientious, diligent, undemonstrative, relatively friendless, truthful and strongly attached to their mothers. Most of them seemed unimaginative, matter-of-fact and logical and orderly in their type of thinking. They were placid, phlegmatic and even-tempered and showed little tendency to brood. Sexual adaptability appeared to be defective in most of the patients. Modesty and prudishness were found in excess. These patients were inclined to be shy in the presence of girls and secretive on the subject of sex. Feelings of inferiority were present, but not to an unusual degree.

DAVIDSON, Newark, N. J.

THE EFFECT OF LIVER THERAPY ON THE NEUROLOGIC MANIFESTATIONS OF PERNICIOUS ANEMIA. BENJAMIN M. BAKER, JR., JAMES BORDLEY, III and WARFIELD T. LONGCOPE, Am. J. M. Sc. **184**:1 (July) 1932.

The literature is reviewed from the standpoint of reports, some showing improvement in the involvement of the nervous system, others not. The authors present 44 cases, 39 showing involvement of the nervous system; of the latter, improvement was noted in 61.5 per cent. Tables are given describing the occurrence of detailed signs and symptoms, with their course as to improvement, depending on the duration of treatment, from two weeks to forty months. In 8 cases of combined degeneration in which the patients were under treatment for ten months or more, 58.9 per cent showed improvement. In an attempt to correlate improvement with the rise in the red blood cell count, it was found that this was not absolute, but that it was noticeable. Five cases are described in detail, exemplifying rather characteristically the claim made by the authors. The improvement is most noted in the sensory disturbances and motor paresis; large quantities of liver are required for the best results, which may take a long time. Previous experiments of other workers suggest that a deficiency in vitamin B might be accountable for the alterations in the nervous system in pernicious anemia.

MICHAELS, Boston.

A CASE OF CORTICAL BLINDNESS. L. RIMBAUD, J. CHARDONNEAU and A. BALMÈS, Rev. d'oto-neuro-opht. **10**:687 (Nov.) 1932.

The case presented in this article is a combination of optic atrophy with cortical blindness. The patient, aged 58, had an attack of giddiness without loss of consciousness or falling in July, 1928. Since then, a sense of fog before the eyes and diurnal headaches had been present. In September, examination revealed no disturbance of the circulatory and nervous systems; visual acuity was slightly diminished, and the pupils reacted to light and in accommodation. On April 1, 1929, complete loss of vision occurred. On examination, complete blindness, feeble pupillary reaction to light and discrete bilateral optic atrophy were revealed. In addition there were right hemiparesis, ankle clonus and abolition of the abdominal reflexes. The patient grew worse and died in January, 1932. At autopsy, total destruction of the inner surfaces of the occipital lobes in the region of the cuneus by yellow softening was observed. No trace of the calcarine fissure nor of the convolutions around it remained. Along the course of the posterior cerebral arteries, from the bifurcation of the basilar trunk to their entrance into the brain, plaques of atheroma that partially obstructed them were found.

DENNIS, Colorado Springs, Colo.

GROWTH FACTORS IN CHILD GUIDANCE. ARNOLD GESELL, Ment. Hyg. **16**:202 (April) 1932.

The mind, like the body, is a growing organism; behavior develops in accordance with laws of growth as inescapable as the laws of gravity. This process of mental growth is no metaphysical abstraction but rather a reality as concrete as nutrition. Of course one cannot see psychic growth as directly as one can note physical development, but the former expresses itself in patterns of behavior which become increasingly purposeful and increasingly complex. The growth of mind is not wholly determined by conditioned reflexes, by subconscious urges or even by habit, but rather by a process of maturation. It is from this standpoint — a relative and a dynamic one — that problems of child guidance must be viewed. One must not view the fabrications of a child aged 4 in the same way that one looks on the lying of a boy aged 17. One needs a kind of "genetic patience," which will enable one to look sympathetically, understandingly and tolerantly on behavior problems that are a parcel of psychic immaturity. Gesell

believes that adolescent children should be taught to recognize this growth process and to cultivate it as part of their personal philosophy. Life in this manner becomes less confused and more meaningful. DAVIDSON, Newark, N. J.

THE RÔLE OF THE PITUITARY GLAND IN PREGNANCY AND PARTURITION: HYPOPHYSECTOMY, H. ALLAN and P. WILES, J. Physiol. **75**:23 (May 30) 1932.

It has been stated frequently that the invariable result of hypophysectomy during pregnancy is immediate abortion. A series of hypophysectomies were performed in pregnant animals to test the truth of this statement. Of the four methods available, only the buccal and retropharyngeal are convenient in the cat. A new operative procedure for the retropharyngeal route is described in detail. A modification of McLearis' procedure for the buccal route is outlined. The earlier operations were followed in many cases by the delivery of normal-looking fetuses in two or three days. At that time it was impossible to obtain pregnant cats for which the dates of impregnation were known, so that there was no evidence that the deliveries were not occurring at the appropriate times. The greatest time observed to elapse after operation before delivery occurred was eleven days. From their results thus far the authors conclude that delivery can take place apparently quite normally in the absence of the pituitary gland, and that delivery does not necessarily follow immediately on removal of this gland. Suckling was not observed to take place.

ALPERS, Philadelphia.

ECONOMIC LOSS TO NEW YORK STATE AND TO THE UNITED STATES ON ACCOUNT OF MENTAL DISEASE, 1931. HORATIO M. POLLOCK, Ment. Hyg. **16**:289 (April) 1932.

As a result of careful statistical study of the cost of maintenance of hospitals for patients with mental disorders in the United States, Pollock concludes that the third of a million of patients in psychopathic institutions are supported at an annual cost of $208,000,000. The loss of future net earnings of these patients is somewhat more difficult to estimate; Pollock established indexes for each type of mental disease, the figures varying from a 45 per cent loss of future earnings in the instance of manic-depressive patients to 95 per cent in the senile group. Patients with dementia praecox or dementia paralytica are estimated to suffer a loss of 75 per cent of their future net income. On this basis, the loss to the country through reduction in earnings of the mentally ill is fixed at $534,000,000. This brings the determinable economic loss due to mental disease to the staggering annual total of three quarters of a billion dollars. [With the addition of the maintenance costs and losses in earnings of the uncommitted insane, the cost of mental disease would probably approximate a billion dollars a year.]

DAVIDSON, Newark, N. J.

CEREBELLOVESTIBULAR DISTURBANCES AFTER CRANIAL TRAUMATISMS. G. MARINESCO and E. FAÇON, Rev. d'oto-neuro-opht. **10**:645 (Nov.) 1932.

In studying a large number of cases of cerebral concussion, the impression is gained that cerebellovestibular disturbances are rare. The authors have determined the chronaxia of the vestibular nerves and modifications of the reflexes of position (*Lagereflexe*) in these cases and observed the following facts: (*a*) In cases with cerebellovestibular symptoms, chronaxia of the vestibular nerves is increased (from 100 to 150 degrees instead of a normal of from 13 to 30 degrees), and the modifications of position indicate cerebellovestibular troubles; (*b*) in cases without cerebellovestibular symptoms but with other nervous manifestations (hemiplegia or convulsive crises) great modifications of the chronaxia of the vestibular nerves and of the reflexes of position exist. In these two groups of cases the classic vestibular tests did not supply conclusive data. It is believed

that the use of this method permits the determination of the organic character of the disturbances. They are thought to be caused by circulatory perturbations that consist of changes in the caliber of the intracerebral vessels. Hence the prognosis is favorable in most cases. DENNIS, Colorado Springs, Colo.

DIMENSIONS OF THE LIVING HEART IN SCHIZOPHRENIA. RALPH G. REED, Psychiat. Quart. **6**:617 (Oct.) 1932.

Measurement of the heart by fluoroscopy and teleoroentgenography fails to substantiate the traditional idea that in persons with schizophrenia the heart is smaller than it is in normal persons. The index for the size of the heart was obtained by combining the width at the base, the greatest width and the length. Two hundred and four physically sound schizophrenic patients were studied, a group of 205 physically and mentally healthy employees being used as controls. The average index for the size of the heart in millimeters was 342 (normal men) as compared with 359 (schizophrenic men). Among women the difference was even smaller, the indexes being 340 and 344 for normal and for schizophrenic women, respectively. The hypoplastic, perpendicularly placed organ (so-called "drop heart") did not prevail in the schizophrenic patients, being found in 11 per cent of the men patients and 17 per cent of the normal men, and 22 per cent of the schizophrenic women and 16 per cent of the normal women. It seems that a study of cardiac size gives no comfort to the supporters of the hypothesis that dementia praecox is associated with constant organic change. DAVIDSON, Newark, N. J.

IMPROVEMENT IN NERVOUS AND MENTAL STATES UNDER CORTIN THERAPY. HARTMAN, BECK and THORN, J. Nerv. & Ment. Dis. **77**:1 (Jan.) 1933.

Hartman, Beck and Thorn discuss the influence of massive doses of 1,200 Gm. of cortin injected subcutaneously in three groups of cases. The first group, Addison's disease with mental disturbances, suggested suprarenal cortical insufficiency; the disturbances consisted of irritability, depression, restlessness, clonic spasm and coma-like reaction. In the second group there were three cases, not diagnosed definitely as Addison's disease, but in which nervous and muscular fatigue occurred without neurologic changes. The third group consisted of five cases in which definite organic neurologic change was accompanied by muscular weakness. In the second and third groups the dose of cortin injected varied from 160 to 300 Gm., daily. In two cases of myasthenia gravis no improvement resulted. In cases of progressive muscular dystrophy and progressive muscular atrophy, fatigue was diminished with a concomitant increase in strength. Myotonic manifestations decreased. Cheerfulness replaced depression, irritability disappeared, and there was improvement in the gastro-intestinal and sleep functions.

HART, Greenwich, Conn.

THE PART PLAYED BY THE SYMPATHETIC SYSTEM AS AN AFFERENT MECHANISM IN THE REGION OF THE TRIGEMINUS. HARRY HELSON, Brain **55**:114 (March) 1932.

In fifteen subjects in whom section of the second and third divisions of the trigeminal root had been made, sensory examinations were performed in order to determine whether or not sensation remains after deprivation of the trigeminal supply. Immediately after operation there is no sense of light pressure, but within a year if a hair or straw is brushed or swept across the face it will be felt. Appreciation of deep pressure returns within a year. Sensation from the medium range of temperatures is lost after operation, but an extremely hot stimulus (between 60 and 75 C.) will be reported as a stinging or pricking sensation. Patients who had also undergone thoracic sympathectomy did not respond to hot stimuli. Normally, the trigeminal nerve alone mediates the sense of pain. Localization improves from absolute inability to an error only twice as great as the normal

error. In view of an afferent path the functions of which are diffuse and totalized, it is believed that this nerve belongs to the sympathetic and parasympathetic systems.

MICHAELS, Boston.

CEREBRAL AND SPINAL FLUID PENETRATION OF BISMUTH. P. J. HANZLIK, H. G. MEHRTENS and JEAN SPAULDING, Am. J. Syph. **16**:350 (July) 1932.

Patients with spinal syphilis who had received electropositive bismuth in the form of the alkaline tartrate seldom showed evidence of the presence of this metal in their spinal fluids even after prolonged treatment. Seventy-three per cent of the authors' patients in this series showed no bismuth in the fluid, although they had varying quantities in the blood stream. With the use, however, of proprietary bismuth-iodide preparations in which the metallic radical is an anion bismuth appeared in the spinal fluids of 83 per cent of the patients. To insure the penetration of the metal into the spinal fluid, the following regimen is recommended: a bismuth-iodide preparation in 2 cc. doses, two treatments weekly for a month. This will yield 160 mg. of injectable bismuth. Under appropriate conditions it is probable that even electropositive bismuth, notably the sodium tartrate, can yield metallic anions, but the primary utilization of the bismuth-iodide preparations is to be recommended because of the dependability of the drug in this form.

DAVIDSON, Newark, N. J.

THE FREQUENT OCCURRENCE OF ABNORMAL CUTANEOUS CAPILLARIES IN CONSTITUTIONAL NEURASTHENIC STATES. J. Q. GRIFFITH, Am. J. M. Sc. **183**:180 (Feb.) 1932.

Capillaroscopic findings by workers in many diverse conditions are reviewed. Of relation to the present study is the concept of Muller, the "vasoneurotic diathesis" in persons who from early childhood have been neurasthenic and unable to cope with their environment. Most significantly their capillaries show fantastically coursing and frequently large forms. In thirty-one of five hundred cases without evidence of organic peripheral vascular lesions, the diagnosis included a functional "neurasthenic" condition; eight cases showed a definitely morphologically abnormal capillary picture. The author concludes that abnormal capillary configurations are most apt to occur in conjunction with neurasthenic states that manifest themselves early in life and are accompanied by vasomotor symptoms. The suggestion of a constitutional nervous instability is offered, and it would seem that these studies are significant in adding weight to the concept of constitution.

MICHAELS, Boston.

HERPES ZOSTER AND POLYNEURITIS FOLLOWING THE ADMINISTRATION OF BISMUTH. S. WILLIAM BECKER, Am. J. Syph. **16**:313 (July) 1932.

Both herpes zoster and polyneuritis are well known but rare complications of bismuth therapy. The author reports one case of each. In one instance bismarsen was employed; in the other, a case of polyneuritis, suspension of bismuth salicylate was used. In the former case, a woman, aged 45, suffered from bilateral syphilitic nerve deafness. Following several injections of bismarsen, herpes zoster developed along one of the left intercostal nerve trunks. The vesicles healed, leaving scars. The other patient, a woman, aged 39, had tabes dorsalis. She was receiving both bismuth (intramuscularly) and arsenic (intravenously). During the course of treatment, about six months after the therapeutic regimen had begun, polyneuritis developed in all extremities. The symptoms persisted for only a few days after the withdrawal of medication, and did not return when bismuth and arsenic were resumed a few months later. The author does not state why he believes that the bismuth rather than the arsenic produced the peripheral neuritis in the second case.

DAVIDSON, Newark, N. J.

FULMINATING MENINGOCOCCAL MENINGITIS. J. N. C. FORD and GEOFFREY SHERA, Brit. M. J. **1**:558 (March 26) 1932.

The authors report an unusual case of fulminating meningococcic meningitis with sudden and acute onset and no history of contact with any other case. At the time of report this was the only case in the district, and no other occurred subsequently. After the initial rise in temperature, there was a comparatively low temperature, which was again normal on the eighteenth day. Rapid improvement resulted from early cisternal drainage and injection of serum. Caution is advised in the injection of serum into the cisterna magna, since in any case some degree of apnea occurs. This is obviated considerably by warming the serum to avoid interference with the respiratory center. The cell count and percentage of organisms in specimens of the cerebrospinal fluid were of prognostic value and determined further serum requirements. Multiple arthritis was noticed on the sixth day of the illness, producing pus in both knee joints, which necessitated aspiration twice. At the end of four months recovery was complete, with no sequelae.

FERGUSON, Niagara Falls, N. Y.

HYDROCEPHALUS: A HEREDITARY CHARACTER IN THE HOUSE MOUSE. FRANK H. CLARK, Proc. Nat. Acad. Sc. **18**:654 (Nov.) 1932.

By mating and interbreeding mice which were descended from stock in which hydrocephalus had appeared, Clark was able to demonstrate statistically that the quality is transmitted in a mendelian pattern as a recessive unit character. The hydrocephalus usually appeared a week or two after birth; the animal would be grotesque in appearance and lacking in coordination. A clear liquid collected above the brain, distending the roof of the skull outward; the brain itself was pushed downward and forward. When the pressure was relieved by incision, the cerebral hemispheres collapsed. In his study, Clark first found hydrocephalus in the back-cross generation of a cross between two flexed-tail males and several nonflexed-tail females. Neither of the parents nor any of their progeny showed signs of hydrocephalus. When the flexed-tail mice of the second generation were back-crossed to the F_1 animals, hydrocephalic mice appeared in some of the resulting litters.

DAVIDSON, Newark, N. J.

RADIOGRAPHIC INVESTIGATION OF LUMBAR AND SCIATIC PAIN. JAMES F. BRAILSFORD, Brit. M. J. **2**:827 (Nov. 5) 1932.

"No symptom or group of symptoms as those known to the lay public under the terms 'lumbago' or 'sciatica' may be due to such a diversity of causes," says the author. A case is mentioned of an aneurysm of the abdominal aorta which caused lumbar pain. Congenital or developmental abnormalities of the lumbosacral region are common; although sometimes they may cause no symptoms, frequently they do. Gynecological difficulties are common causes, either directly or from toxic or infectious changes which they cause in the spine. Trauma in a young person may produce no symptoms, while in an older person a less severe injury may provoke much pain and distress. Acute lumbar and sciatic pain is most frequently associated with toxemia from some focus of septic absorption, such as in the teeth, the colon, the genito-urinary system, the appendix, the gallbladder or the sinuses. Tumors and new growths of all types, either primary or from metastatic involvement, constitute still another cause of lumbar or sciatic pain.

FERGUSON, Niagara Falls, N. Y.

ENDOCRINE THERAPY IN THE PSYCHOSES. R. G. HOSKINS and F. H. SLEEPER, Am. J. M. Sc. **184**:158 (Aug.) 1932.

The authors believe that, besides psychogenic factors, in the origin of schizophrenia there is also a constitutional liability factor. Morphologic stigmas are more often found in schizophrenia than in normal persons. The basal metabolic

rate is depressed over 10 per cent, and the blood pressure about 10 per cent. The literature is cited to show the relationship of personality changes to defects of the glands — the thyroid, gonads, pituitary and parathyroids. According to the authors there is much probability that the psychoses are significantly correlated with endocrine deficiencies. Previous work dealing with endocrine therapy is reviewed, and deficiency of the suprarenal cortex is suggested as the characteristic metabolic picture in schizophrenia. From studies with thyroid therapy it was also thought that thyroid deficiency plays a significant rôle in more than 10 per cent of hospital cases of dementia praecox.

MICHAELS, Boston.

MENTAL ALLERGY. J. H. BLAISDELL, Arch. Dermat. & Syph. **25**:205 (Feb.) 1932.

The importance of emotional states in the chemical composition of the body is emphasized by Blaisdell, who cites the case of a woman in whom seborrheic eczema developed under the influence of great affective stress. Shortly after marriage, which proved to be sexually inadequate and financially insecure, a rash developed. When the emotional strain was eased by separation from her husband, the eczema vanished. Repeatedly the renewal of psychic stresses caused a reoccurrence of the dermatosis. On one occasion, following a narrow escape from serious injury in an automobile accident cutaneous lesions developed. On other occasions letters of emotional significance would suffice to precipitate a rash within a few hours of receipt of the letter. The need of a physician's understanding the entire personal make-up of the patient, as well as his need of comprehending immediate physical disorders, is stressed.

DAVIDSON, Newark, N. J.

FLEXION REFLEX OF THE LEGS IN LOCALIZATION OF CEREBRAL LESIONS. J. ROTHFELD, Nervenarzt **5**:528 (Oct. 15) 1932.

In the presence of cerebral disease, flexion of one leg at the knee and hip or, better, raising of the leg while it is held straight, as in the Lasègue test, may cause the other leg to flex at the hip, knee and ankle. In three cases of tumor of the frontal lobe studied by Rothfeld, flexion of the leg on the side opposite the lesion could be elicited in this manner, but in seven cases of lesions of the parietal or temporal lobe, some of which involved the basal ganglia, only the leg on the same side as the lesion could be caused to flex. Flexion could be elicited in either leg in a case of frontoparietal tumor, although the reaction was more pronounced on the side of the lesion. A bilateral response may also be obtained when the lesion involves symmetrical portions of both hemispheres. The presence of the reaction on one side, therefore, indicates involvement either of the contralateral frontal lobe or of the homolateral parietotemporal lobe. If the side involved can be determined by other means, it is possible to predict from this test whether the bulk of the lesion is in the frontal or retrofrontal region.

DANIELS, Denver.

THE ENDINGS OF CALLOSAL FIBERS IN THE CEREBRAL CORTEX. J. M. DE VILLAVERDE, Trav. du lab. recherches biol. de l'Univ. de Madrid **27**:275, 1931-1932.

Villaverde had already examined by the Marchi method the endings of the callosal fibers in several fields of the cerebral cortex of the rabbit, but since this method did not give complete information he used the anatomic methods (Pal, Cajal, Golgi) in the area retrosplenialis and peristriata of the mouse and the area limbica of the guinea-pig. The callosal fibers give rise, by means of collaterals, to an important part of the plexus in the fifth layer (large pyramids), but end in the superficial layers. The different fields of the area retrosplenialis are also characterized by the number and distribution of the callosal fibers they receive.

LORENTE DE NÓ, St. Louis.

A Lesion of a Cerebral Hemisphere with Induced Nystagmus on the Healthy Side. Buys, J. de neurol. et de psychiat. **32**:717 (Oct.) 1932.

Buys reports the case of a patient with a destructive lesion of the left cerebral hemisphere following trauma, associated with disturbance of the semicircular canals and characterized by induced nystagmus, which was more marked on the healthy side. It is stated that this induced nystagmus was of central origin, first shown by the agreement of results of the rotation and thermic Bárány tests, all producing a nystagmus which was more severe on the healthy side. The author reports from the literature that following experimental ablation of the cerebral hemisphere in the rabbit induced nystagmus was more intense on the side of the lesions. It was found that in tumors and abscesses induced nystagmus was obtained more easily on the side of the lesion.

Waggoner, Ann Arbor, Mich.

A Case of Recklinghausen's Disease. J. W. Kernohan and H. L. Parker, J. Nerv. & Ment. Dis. **76**:313 (Oct.) 1932.

Kernohan and Parker, describe in detail a case of Recklinghausen's disease in which, besides the neurofibromatosis, there were numerous meningiomas and four distinct gliomas of the spinal cord. The latter belonged to the types of astrocytoma and cellular ependymoma. There was also a syringomyelia, with a presyringomyelic stage at each end of the cavity. The neurofibromas of the cranial nerves and dorsal roots did not quite conform to the types of tumors supposed to be present in these situations in Recklinghausen's disease. The case also illustrates the continuous tendency to form new tumors in varying situations, and the inevitably poor prognosis.

Hart, Greenwich, Conn.

Efficacy of Bismarsen in Wassermann-Fast Syphilis. J. L. Grund, Arch. Dermat. & Syph. **26**:1074 (Dec.) 1932.

Each of three patients with Wassermann-fast syphilis received an intensive course of treatment with bismuth arsphenamine sulphonate (bismarsen). None presented any serologic changes in spite of the administration to each of forty injections of the preparation. Grund presents this series as confirmatory of previous reports that bismarsen has no especial value in Wassermann-fast syphilis. While the number of cases presented is too small to demonstrate any positive value or inutility, Grund would add his cases to the number already recorded in the literature—a number sufficiently large to offer a fair basis for the evaluation of the drug.

Davidson, Newark, N. J.

Ontogenetic Development of the Calcarine Cortex. Benjamin Pushkin, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **34**:48, 1932.

The development of the calcarine cortex is so far advanced in the sixth month of embryonal life that its six layers can be definitely distinguished, while in the adjacent cortex a differentiation of layers is barely visible. It would seem that the early differentiation in the calcarine cortex bears some relationship to the formation of the convolutions in this cortex, because the layers of the convolutions that appear early (the primary convolutions) are developed much more than those of the convolutions that appear later, i. e., the secondary convolutions.

Keschner, New York.

Psychoses and Tumors of the Pituitary Body. E. Meumann, Arch. f. Psychiat. **96**:609 (April) 1932.

The author presents two cases of acromegaly with pituitary tumors (in the first case proved by exploration and in the second by autopsy), in which mental disturbances were associated with the neurologic symptoms. These disturbances were of a chronic type and characterized by hallucinatory and delusional phenomena.

Superficially they resembled the paranoid type of dementia praecox, but closer analysis showed definite differences. The development of these psychoses and their relationship to organic disturbances on the basis of the growth of the neoplasms are discussed.

MALAMUD, Iowa City.

THE HEMATOPOIETIC RESPONSE IN PERNICIOUS ANEMIA FOLLOWING THE INTRAMUSCULAR INJECTION OF GASTRIC JUICE. ROGER S. MORRIS, LEON SCHIFF, GEORGE BURGER and JAMES E. SHERMAN, Am. J. M. Sc. **184**:778 (Dec.) 1932.

Normal human gastric juice, concentrated by distillation in vacuo, was given intramuscularly to patients with pernicious anemia and resulted in a reticulocytosis and maturation of the red blood cells. Pain at the site of injection is the most untoward symptom. The authors propose the name "addisin," after Thomas Addison, for the anti-anemic substance of gastric juice, which is described as being thermolabile, dialyzable and exhaustible, and which is probably a hormone.

MICHAELS, Boston.

NEURITIS AND MULTIPLE NEURITIS FOLLOWING SERUM THERAPY. GEORGE WILSON and SAMUEL B. HADDEN, J. A. M. A. **98**:123 (Jan. 9) 1932.

Among the complications of serum therapy, neuritis and multiple neuritis occasionally occur, and are regarded as types of anaphylaxis. The majority of cases follow the injection of tetanus antitoxin, although some have developed following the administration of diphtheric antiserum and, more rarely, of antistreptococcic serum. The brachial plexus, especially the upper cord, is most frequently involved. Six cases are reported.

JENKINS, Indianapolis.

ARACHNITIS ADHESIVA CIRCUMSCRIPTA IN A PATIENT WITH LATE RACHITIC DEFORMITY OF THE VERTEBRAL COLUMN. R. GRÜN, Ztschr. f. d. ges. Neurol. u.Psychiat. **138**:428, 1932.

Arachnitis has been described as secondary disorder in a number of conditions —acute and chronic infections, inflammations, tumors and injuries of the spinal column, the spinal cord and its membranes and infection of the nervous system. In addition to these there is a group of cases of unknown etiology, spoken of as the primary form of arachnitis. Grün reports a case of this type which occurred in a patient with late rachitic deformity of the vertebral column.

ALPERS, Philadelphia.

THE HISTOLYTIC AGENTS OF THE NERVOUS SYSTEM OF THE TAIL OF THE TADPOLE. DOMINGO SANCHEZ Y SANCHEZ, Trav. du lab. recherches biol. de l'Univ. de Madrid **27**:299, 1931-1932.

During the metamorphosis of insects, Sanchez found that the nervous system of the pupa disappears totally, and that the insect acquires a new one. The disappearance of the old nervous system is due to histolytic processes, not to phagocytosis. It is shown now that the regression of the nervous system of the tail of the tadpole similarly is due to histolysis.

TECHNIC FOR STAINING WITH ETHYL-AMINE-SILVER OXALATE. J. M. HERRERA BOLLO, Trav. du lab. recherches biol. de l'Univ. de Madrid. **27**:325, 1931-1932.

It is proposed to use ethylamine-silver oxalate in the methods of Bielschowsky, Cajal and Rio-Hortega. The author claims that the results are as good as with the original methods; as a fact, the photomicrographs in the paper show splendid stains of connective tissue, epitheliofibrils, glia cells and microglia.

SYMPATHETIC CELLS WITH SEVERAL NUCLEI. A. TSCHERNJACHIWSKY, Trav. du lab. recherches biol. de l'Univ. de Madrid **27**:249, 1931-1932.

Sympathetic nerve cells with two or more nuclei are not rare. Drawings and photographs of such cells are given and, in addition, a complete bibliographic notice of similar findings.

THE NERVE ENDINGS IN THE EPITHELIUM BETWEEN THE SWEAT GLANDS. A. P. RODRIGUEZ-PEREZ, Trav. du lab. recherches biol. de l'Univ. de Madrid **27**:339, 1931-1932.

Using the Cajal method, the author stained already known intra-epithelial endings in the skin of the foot of man and cat.

LORENTE DE NÓ, St. Louis.

Society Transactions

NEW YORK NEUROLOGICAL SOCIETY

Regular Meeting, Oct. 3, 1933

HENRY ALSOP RILEY, M.D., *President, in the Chair*

THREE CASES OF MULTIPLE NEUROFIBROMATOSIS. DR. ARTHUR H. JACKSON, Washington, Conn.

As it has been generally considered that the malignant degeneration occurring in multiple neurofibromatosis or Recklinghausen's disease is a comparatively rare occurrence, it may be of interest to report three cases of that disease observed during a period of three years in the hospitals of New Haven and Waterbury. The three cases, moreover, presented other features of this disease which were of more than usual interest.

CASE 1.—A woman, aged 43, was admitted to the surgical service of the New Haven Hospital for the first time in August, 1929, with the complaint of severe pain in the left leg. Her body was covered with hundreds of small tumor masses, some of which were sessile and others pedunculated. In the left iliac fossa was a hard mass as big as an orange, pressure on which caused "pins and needles" sensations in the left knee. At operation it was found that this tumor involved the femoral nerve. It was removed without difficulty; pathologic examination showed it to be a neurofibroma. The removal of this tumor gave the patient complete relief from all symptoms.

She was readmitted nine months later; she had been unable to walk for three months and was suffering from severe pain in the left leg and in the lower part of the back on the left side. At this time there was an area of anesthesia involving the anterior surface of the left thigh down to the knee, and the left knee jerk was absent. The entire left side of the abdomen was filled with a firm, smooth, immovable and slightly tender mass which at operation proved to be 14 by 9.5 by 8 cm. This tumor involved the femoral, the lateral femoral cutaneous and the obturator nerves of the left side and three cords of the lumbar plexus. It was removed, but the patient died on the operating table. On pathologic examination the tumor proved to be a neurosarcoma.

CASE 2.—A boy, aged 14, was the third and youngest child of the aforementioned patient. He was admitted to the Waterbury Hospital in February, 1931, complaining of shortness of breath, difficulty in walking and poor posture. He was an ill-developed, badly nourished boy with a marked skeletal deformity. The head was drawn over toward the right shoulder, there were marked lordosis and scoliosis, with a reversed curve of the cervical region. The left arm was considerably larger than the right and presented the picture of a plexiform neurofibroma. The tissues of the left breast were pendulous, and the skin in that area was purplish. The condition resembled a hemangioma. Hundreds of small brownish spots were scattered over the entire body. The tissues of the breast and left arm had a wormlike feeling. In the left supraclavicular space was a stony hard, insensitive mass, which seemed to push the head over to the right. The patient became dyspneic on slight exertion and had a hacking cough.

Examination of the eyes, nose, throat, heart and abdomen gave negative results, but there was dulness in the second and third intercostal spaces; breathing was rather forceful throughout. No râles were heard. The left radial pulse was definitely weaker than the right. The strength of the muscles was reduced equally on both sides. The patient was evidently abnormal mentally; no psychometric

tests were made. Endocrine deficiency was evidenced by the undeveloped sexual organs and the entire absence of pubic and axillary hair.

Roentgenographic examination of the spine and long bones showed no evidence of subperiosteal cysts, but many of the vertebrae had a peculiar moth-eaten appearance. Pictures of the thorax revealed tumor masses of soft tissue at the apexes of both lungs. Biopsy of one of the small tumors of the arm showed a typical neurofibroma. A year later the boy was definitely worse. It was believed that the mass at the apex of the left lung was a neurosarcoma.

CASE 3.—A woman, aged 52, was admitted to the Waterbury Hospital in February, 1932. For a year prior to admission she had had weakness of the right foot and pain in the left shoulder. Many brownish spots were scattered over the body; several small cutaneous nodules were also present. There was also a large mass in the left upper quadrant of the abdomen. A spinal puncture, done on admission, revealed no evidence of block. Two days later paralysis of the muscles of the abdomen and both lower extremities, with complete loss of sensation below the seventh thoracic dermatome, developed. Roentgenographic examination showed marked absorption of the sixth thoracic vertebra; this was believed to be due to a malignant process. The abdominal mass grew until it filled a still greater part of the abdomen. A large mass, which apparently represented further growth of the tumor, appeared in the back, causing destruction of the vertebra.

One of the small tumors was removed for study; microscopic examination showed the presence of many malignant tumor cells of the giant type with bizarre-shaped single and lobulated nuclei; some mitotic figures were also found. The patient died about two weeks before this presentation, but unfortunately no autopsy was done.

Case 1 demonstrated the rapidity with which a large malignant tumor can develop. Case 2 was interesting in many ways, but chiefly because of the peculiar changes in the bones. A careful review of the literature failed to disclose a comparable case. Case 3 was of special interest because of the presence of several malignant tumors; when malignant changes occur in multiple neurofibromatosis they are usually confined to one tumor.

DISCUSSION

DR. JOSEPH H. GLOBUS: Unquestionably these three cases are very unusual. I recall a case of Recklinghausen's disease with a malignant process in the chest studied at the Mount Sinai Hospital. It was very similar to one of the three cases described by Dr. Jackson. There was another case which was not followed up as carefully as the first. These reports suggest that the disease is not as infrequent as the literature indicates.

I wish to make another remark in regard to the term "neurofibroma." If I were to be guided by the slide which was shown, I should be more inclined to call the condition a schwannoma. The sections indicate a form of glia cell growth, with no production of nerve fibers.

DR. LOUIS D. ARONSON: Dr. Jackson has brought up an interesting question. The second patient evidently presented many anomalies of osseous development, and probably many of the internal secretory glands did not function normally. The first and second cases had something in common. Dr. Jackson mentioned that a diagnosis of malignant changes was made following roentgenographic examination and biopsy. It struck me several years ago that occasionally it is possible to suspect the presence of malignant changes in tumors in Recklinghausen's disease without laboratory aid; I have in mind a case studied at the Mount Sinai Hospital about eight years ago. A young woman had typical neurofibromatosis; a mass appeared in the eighth thoracic vertebra. This was diagnosed as a sarcoma, irrespective of the fact that the patient had Recklinghausen's disease; biopsy proved that the diagnosis of sarcoma was correct. The question of the probability of malignancy involves pigmentation and hairy overgrowths. In Dr. Jackson's

last case there was a great deal of pigmentation. When one finds a recent deposit of pigmentation in some of the macules, and especially pigmentation of a little hairy growth, one has a clinical reason for suspecting that a new tumor is a sarcoma and not an ordinary neurofibroma.

DR. GEORGE H. HYSLOP: I think that the textbooks of pathology have pointed out that it is not uncommon to find other ectodermal defects associated with neurofibromatosis. Mesodermal defects are also occasionally associated with Recklinghausen's disease. The coexistence of spina bifida with this disease was reported many years ago. The second case described by Dr. Jackson, that presenting a mass in the neck, perhaps belongs to a group of cases of cervical neurofibromas, first described by a French author in 1923. Two years ago, in one of the cases of multiple neurofibromas seen at the Memorial Hospital there was one in which multiple symmetrical nevi, a syringomyelic picture and multiple bony cysts were present.

DR. LEWIS D. STEVENSON: At the Bellevue Hospital I have seen one case with sarcomatous degeneration in a tumor situated on the back of the neck. In general, when Recklinghausen's disease becomes malignant sarcoma results. I should like to ask whether any nerve fibers were found in any of the tumors, a point stressed by Penfield. It seems to me that growths which have nerve elements cannot be classed as tumors.

DR. ARTHUR H. JACKSON: Nerve tissue was present in cases 1 and 2. In case 1, nerve fibers were found both in the benign tumor that was removed first and in the malignant tumor. In case 2, nerve elements were found in the biopsy specimen.

Dr. Aronson has spoken of the discolorations that appear. The first patient, the mother of the second patient, had pigmented spots all her life. The second patient, who shows more spots than any of the others, had shown these discolorations only for five or six years before he came to us. The third patient, who also presented a definitely malignant condition, had very few brown spots; so far as we know, these had been present all her life.

NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY, AND NEW YORK SOCIETY FOR CLINICAL PSYCHIATRY

C. BURNS CRAIG, M.D., *Secretary*

Joint Meeting, Oct. 10, 1933

CLARENCE P. OBERNDORF, M.D., *Chairman*

PHYSICAL COMPLAINTS DISGUISING FANTASIES OF PREGNANCY. DR. NORVELLE C. LAMAR.

A girl, aged 15, has been under treatment at the Payne Whitney Psychiatric Clinic. The complaints were: headaches, wakefulness at night, refusal to continue with school work, many vague fears and a number of aches and pains. The family consists of the parents, a sister of 18 years and the patient. The sister is attractive, intelligent and popular. Although affectionate toward the patient she assumes a superior attitude.

The patient, a quiet, conscientious child, had been troubled with stubborn constipation all her life. She made good progress in school and was well liked. Two years before admission she began to be restless and to have difficulty in sleeping. Examination showed nothing of note except a spastic stomach, which soon relaxed. In the hospital the patient adjusted herself quickly and the constipation disappeared without medication. Several themes were found running in tangled fashion through

her neurosis, including extreme jealousy of her sister, at first unconscious, and fears and delusional ideas concerning catamenia and pregnancy, which were connected with possible injury. After five months of treatment she began to have distressing pains in the abdomen, which were interpreted as fantasies of parturition. Under psychotherapy all the symptoms disappeared.

DISCUSSION

DR. HARRY M. TIEBOUT: I am acquainted with the patient. She is now doing very well. She is making a fair adjustment at home with the family. She is back in school, has lost practically all symptoms, and is actually now forming an attachment for a young man. I am not sure that Dr. LaMar emphasized how serious this illness seemed to be before the patient was admitted to the hospital.

I raise the question about the value of her coming to stay in the hospital. Was there any specific value in hospital care in this case? The value to the patient and to the family is that she was in the hospital under the care of people in whom she and they had confidence. There is a tendency to use outpatient departments for shopping. Parents, particularly, cannot see any use in a psychiatrist's talking to children in a clinic. They have talked to the patient themselves. They are critical if they do not see prompt and rapid improvement and are apt to go somewhere else. So from the point of view of the parents the twenty-four hour regimen has value, and it has even more value from that of the children.

This youngster, although she had all her life had bowel movements only once every six or seven days, was having daily bowel movements within the first two weeks of her stay in the hospital without medication and without any pressure on the part of the nurses and doctors. She fitted into a regimen in which she was happy and contented. All that helped to overcome a negative feeling that she had not only for the sister but also for the mother. I wonder if the therapy would have been as effective if she had been in an environment in which there was no opportunity for a positive reaction. Another thing which had an effect on this girl was the socializing experience of the twenty-four hour regimen. From a shy, bashful young girl, she blossomed into a happy, contented, outgoing youngster during the seven months in the hospital.

In outpatient departments for children one never knows whether the stories they tell of the happenings of the day are facts or rationalizations of their own desires. When the child is in the hospital twenty-four hours a day one has an opportunity to see what is going on in him, to what he reacts, and how he reacts. One can control the situation and be in a better position to know the facts and to make interpretations more accurately.

A CATATONIC SYNDROME ASSOCIATED WITH DIABETES MELLITUS. DR. SIGFRIED E. KATZ.

A Jewish girl, aged 24, was admitted to the Presbyterian Hospital in a state of coma and later was transferred to the New York State Psychiatric Institute. She responded well to medical treatment, but remained at times rigid and negativistic, and assumed catatonic postures. She had been of normal intelligence and her adjustment to people had always been good. Her personality had been of the extrovert type.

In March, 1929, a diagnosis of diabetes mellitus was made. She reacted well to diet and to insulin therapy. Two days before admission she began to act peculiarly. On admission she was stuporous and drowsy, and the urine showed sugar, acetone and diacetic acid. She improved at first under treatment with insulin, but soon became unresponsive and resistive. At times she would talk rather freely and then relapse into a catatonic state. Apparently she was hallucinated.

The diabetic condition improved under insulin therapy, but in spite of this the patient remained confused, unresponsive and catatonic. She expressed delusional ideas. On a diet of 100 units of carbohydrate, 70 of protein and 100 of fat, together

with insulin, the patient gradually improved, although she had two severe reactions to insulin. After five months she was discharged as cured. The mental picture had features of a toxic psychosis and also of dementia praecox of the catatonic type.

METABOLIC CONSIDERATIONS REGARDING DIABETIC PSYCHOSES. DR. MEYER M. HARRIS.

Since the discovery of insulin a train of symptoms referable to the nervous system and other organs of the body has been recognized as resulting from insulin or spontaneous hypoglycemia. This observation has indicated the importance of the metabolism of carbohydrate for the proper functioning of the nervous system. Hypoglycemia may affect the vegetative nervous system, producing sweating, flushes, pallor, dimness of vision and the like. The central nervous system may be widely involved, producing general symptoms of headache and fatigue or symptoms which indicate probable involvement of one or more of the following systems: bulbopontile corticospinal and striothalamic. There may be variegated psychic disturbances.

In view of this marked effect on the nervous system resulting from reduction in blood sugar, one expects that diabetes, in which the utilization of sugar is interfered with, will similarly produce marked effects on the central nervous system. This, as clinical experience indicates, is not the case. This apparent paradox may become intelligible in the light of experiments of the last few years regarding the metabolism of the nervous system.

Himwich and Nahum found that in normal, depancreatized or phlorhizinized dogs, although the respiratory quotient ranged between 0.67 and 0.71, depending on the nutritional state of the animal, still the respiratory quotient of the brain was 1 as determined by an analysis for carbon dioxide and oxygen of samples of the blood entering and leaving the brain. This indicated that the brain, even of the experimentally diabetic animal, burned carbohydrate as its chief source of fuel. They also found that in most cases lactic acid and dextrose were removed from the blood stream by the brain.

In studies on human beings Lennox found that the respiratory quotient of the brain was about 0.95, as determined from the carbon dioxide and oxygen content of blood from an artery and the internal jugular vein. The respiratory quotient of the extremities was from 0.72 to 0.77, determined at the same time by analysis of blood from the cubital vein. He also found, as did other investigators, that dextrose in blood from the internal jugular vein was considerably reduced. This is in keeping with the finding of Himwich that the brain uses carbohydrates as its chief source of fuel, while other organs may be using chiefly fat.

It is known that the brain can produce lactic acid from dextrose very rapidly, and also that in the presence of oxygen lactic acid rapidly disappears.

Holmes showed by experiments in vitro that the consumption of oxygen by the gray matter of the brain increases on the addition of dextrose. However, if sodium fluoride is added, which is known to inhibit markedly the formation of lactic acid, dextrose produces only a slight increase in the consumption of oxygen. If lactate is substituted for the dextrose under conditions in which the formation of lactic acid has been interfered with, the consumption of oxygen again markedly increases. Holmes concluded that dextrose must be converted into lactic acid before it can be oxidized by the gray matter. Although the substance oxidized is, in great part, lactic acid, this acid is by no means the only substance oxidized by the brain. Peters and van Slyke stated that in diabetic patients, even those with characteristics of total diabetes (a globulin-nitrogen quotient of 3.6), dextrose can probably be converted into lactic acid, and Barr and his co-workers have shown that a person with moderately severe diabetes can produce lactic acid during exercise. The evidence seems to indicate, therefore, that the brain of the diabetic person can probably utilize carbohydrate even though the organism as a whole shows evidence of disturbance in this form of metabolism by hyperglycemia, glycosuria and other mani-

festations. These considerations may give a clue as to why hypoglycemia produces such marked and sudden mental symptoms, so different from what one sees in the diabetic patient.

It may be of interest to add in this connection that Holmes also demonstrated a poverty of lactic acid in the brains of hypoglycemic animals.

It is therefore doubtful whether the disturbance in the metabolism of carbohydrate seen in mild or moderately severe diabetes will, per se, produce a disturbance in brain function, with mental symptoms. As diabetes becomes very severe, an additional train of metabolic disturbances beside that of the metabolism of carbohydrate sets in, which accounts in part for the marked disturbance in the physiology of the patient. These consist in the formation of large amounts of acetone, diacetic acid and *beta*-hydroxybutyric acid, which are accompanied by loss of base from the body together with disturbances in the distribution of electrolytes in the body. It is questionable whether the acetone bodies, in themselves, produce any markedly injurious effects, although they do have certain physiologic effects as is seen in their favorable effect on certain convulsive states. The disturbance in the inorganic constituents of the body just mentioned is important, for it produces symptoms such as dyspnea and disturbance in circulation, and also in part accounts for the symptoms of diabetic coma.

It is likely that only in very severe diabetes may the mental state be the result of the immediate effect of the disease, and that only in the final stages.

It is indeed doubtful whether in cases of so-called diabetic psychosis in which the diabetes was not severe any causal relation existed between the diabetes and the psychosis. The existence of various types of diabetes is likely. Even earlier clinicians differentiated "neurogenic diabetes" from "constitutional diabetes." However, it is questionable whether such types alter the general metabolic considerations. I am not concerned in this presentation with the glycosuria which may follow pathologic processes in the brain, commotio cerebri due to trauma or to psychic trauma. I am concerned here primarily with psychoses developing in patients with diabetes of long standing and the possible causal relationship of the metabolic disturbance.

It is of interest that the mental aberrations that occur in the psychoses are similar to those one sees frequently in hypoglycemic states but seldom in diabetes.

DISCUSSION

DR. CLARENCE O. CHENEY: The record of this young woman shows that on or about Oct. 31, 1932, she was at Vanderbilt Clinic, apparently in an adjusted diabetic condition, that is, with no sugar and no acetone or diacetic acid in the urine, and was apparently getting along as well as she had at any time. Within thirty-six hours she was admitted to the Presbyterian Hospital in a state threatening diabetic coma. In reviewing the history I thought that something rather important must have happened to her in the interval between her appearance in the clinic and her admission to the hospital. I did not know what had happened until this evening when she told me that she had, during this interval, seen the motion picture "When Life Begins." The scene of the picture is laid in a maternity hospital, with detailed representations of almost everything that goes on in such a hospital. The main character in the picture is a woman who was charged with murder and was brought from the jail by a none-too-sympathetic matron to the hospital to have a child. The question, of course, was whether it was worth while for her to try to live, because she was under a death sentence. There was also the situation of a psychotic woman in the hospital who thought that every child was her own and wandered around the wards trying to pick up the children and carry them off to her own bed.

I was curious, after having seen this picture, to know how it would affect some women who saw it. This is the first experience I have had with a woman who saw it. One might speculate as to what the physiologic effect of the picture was on the patient. She tells me that after seeing it she went home in a rather confused state and in trying to do her housework had a good deal of difficulty in concentrating. She came to the hospital confused twenty-four hours later, with symp-

toms threatening diabetic coma and symptoms of a catatonic state much like that seen in hypoglycemia. We thought at first that she was hypoglycemic and she was treated for that. However, she was found to be not hypoglycemic but hyperglycemic. Such symptoms are not frequent with hyperglycemia.

We thought that she had a reaction which had definite organic elements in it, in that she showed confusion and difficulty in concentration; she still has an amnesia for part of her residence in the hospital. We call the condition toxic, but that is a poor word. There are no actual toxins in diabetes. It is really a metabolic disturbance, and a case of this kind calls attention forcibly to the importance of metabolic studies of most if not all psychiatric patients. The studies presented by Dr. Harris particularly emphasize the fact that the brain is saved by nature in diabetes mellitus, by being able to oxidize dextrose and carbohydrates beyond the point at which other organs in diabetes can oxidize them. That shows how much may be contributed by biochemical and physiologic studies, and is instructive in considering the psychotic reactions associated with metabolic disturbances. They may not have been as impressive in the past as they may be in the future. Some persons think that a great deal of advance in psychiatry may be through physiologic and biochemical studies; this case indicates such a possibility.

What the prognosis is or will be with this girl I am not certain. There is some evidence that she may not have been as well adjusted a personality before the illness as Dr. Katz has indicated. Some one called her a "moral imbecile." I do not know what he meant. The statement may have been made on the basis that she admitted auto-erotic practices, and that she had been going around with boys and may have been intimate with one. That may be one person's idea of moral imbecility; it is not held by all. I think that the diabetes broke down her integrations, which perhaps had been on the ragged edge of breaking down for some time, and that although she showed some organic symptoms the catatonic symptoms were a reaction of her personality, her constitution and her trend of thought. She presented certain symptoms which one sees in combined organic and constitutional reactions. I do not think that one can say at present that there is a characteristic diabetic psychosis. The condition which Dr. Harris described is associated with hypoglycemia. It shows catatonic symptoms or features very often, but as he indicated conditions of hyperglycemia are not often associated with psychotic reactions or catatonia. Therefore, I think that one may say that this girl had a reaction colored by her own personality, which happened to be the type in which a catatonic syndrome would develop.

PSYCHIATRIC PROBLEMS IN CHILD MURDERERS. DR. LAURETTA BENDER.

There are two psychiatric problems related to the murder of offspring or infanticide: (1) that of the mental mechanism that leads to the act; (2) that of the reaction to the deed. Several studies have come from the Broadmoor State Criminal Lunatic Asylum in England which show that the majority of infanticides were performed by mothers who post partum or during lactation succumbed to confusional psychoses in which known suicidal preoccupations were often present before the deed was done, so that the original idea was suicide and not murder. In the psychiatric division of Bellevue Hospital and in the Kings County Hospital there have been observed several psychoses other than postpartum or lactational psychoses, associated with murder or attempted murder of offspring.

In the manic-depressive psychoses, a depressive reaction may lead a mother to attempt suicide together with murder of her children.

CASE 1.—A mother of three children, aged 36, eleven years ago witnessed the accidental death of a son aged 3, as he was struck by a truck in front of the house. Her husband accused her of neglect. She responded with a depression lasting for several weeks; after that she and the husband did not get along well. She had never loved him and now she constantly accused him of insufficient ambition to raise the family above their poor social level. At the same time he often reproached her for the death of their son. She had frequent depressive episodes in which she threatened death for herself and two remaining children. In 1933

she became infatuated with a married man and it was arranged between them that the husband should leave home in order that this man might move in as a boarder. The patient was apparently happy for a time until it became apparent that her daughter, aged 16, had become pregnant by this man; following this discovery the daughter and the man ran away. In a recurrence of the depressive reaction the mother turned on the gas, with her remaining child, aged 11, in bed with her. The two were revived and the patient was charged with felonious assault. She continued to be depressed, but as the husband offered to reunite the family and the daughter returned home, the patient became cheerful and has showed little evidence of remorse.

Here, the death of one child, on account of which she was blamed for negligence, led to depressive reactions and threats of suicide. She finally escaped her husband's repeated accusations by accepting a new lover, and thereby exposed her daughter to a seducer. A recurrence of depression led to a suicidal act which involved the one remaining child. Recovery was rapid when the family was reunited.

More complicated mechanisms involving identification of parent with child and suicidal and homicidal impulses are seen in schizophrenic persons.

CASE 2.—A married woman, aged 29, who had one child, aged 3, was always a "shut-in" personality and was discontented after marriage. After the birth of the child she showed undue anxiety for its well-being and became more seclusive and melancholic. She sat and stared into space and neglected herself and the child. For a year she spoke of being talked about and looked at on the street. She said that she was changing, that her eyes were becoming "starey," that she was losing her mind, and that voices told her about these things. She also said that the child had changed owing to the influence of her eyes on it; that its face was also changing, and that it was becoming smaller instead of larger. She attempted suicide and attempted to kill herself and the child, and attempted to choke the child several times before she finally succeeded in choking it to death. For a day she was depressed; then she passed through a Ganser syndrome for several days in which she denied her own identity and denied that she had ever been married or had a child. Then she remained in a deathlike stupor for a month and emerged from this with an amnesia for the act of choking the child and for the stupor. However, she described her previous symptoms of ideas of reference, auditory hallucinations and feelings of being changed herself, and that through her the child was also changed. She claims that she is now cured of these symptoms. She remains dazed and retarded, with a flat staring facial expression and an inadequate emotional response.

This mother projected her own schizophrenic symptoms into her child, passed through a Ganser syndrome and a reaction of stupor and emerged with no memory of the homicidal act or of the following reaction, and with a feeling that she is cured of her former symptoms.

CASE 3.—A mother who for two days felt the approach of a mental illness and rebelled against it threw her child, aged 9, out of the window as a "gift to God." Afterward the deed was inexplicable to her, and was followed by a rapidly developing catatonic excitement in which she fought off all medical and nursing care until she died three weeks after the death of the child. From a psychologic point of view the death may be considered suicidal. Just before death she said that her whole family, including her husband, also were dead.

CASE 4.—A schizophrenic colored woman felt for some time that she and her two small children were persecuted. In the panic of a fire, which she probably ignited, she misinterpreted the intent of the people who came to her rescue, and in an effort to escape from them attempted to throw herself and the two children from the fire-escape. Only the baby, aged 5 months, was killed. She was never able to recognize what had really happened and reacted by a rapidly developing catatonic excitement.

CASE 5.—A father of two children was an inadequate, delinquent person. He frequently embezzled money and forged checks. His family usually protected him, although he served two prison terms. He was on parole from the last term when

he again forged checks and his mother-in-law threatened to expose him and have him returned to prison. After a night of argument over the subject and broken sleep, he arose and killed his son, aged 7, by slashing the boy's wrist and smothering him in the room in which his wife and a son aged 2 were still sleeping. He claimed that it was his intention to kill the whole family, including himself, in order to have peace for them all, because he could not bear to be separated from them again by another prison term. However, the younger child awoke and called him "Daddy" and stopped him. He waited until his wife awoke and discovered the deed and then he ran away and hid, hoping that what he had done was not true until he read an account of the episode in a newspaper. He intended to commit suicide, but gave himself up. He was emotionally dull and finally depressed for some months, but gradually recovered.

The cases show the tendency for parents, especially mothers, to identify themselves with their children, at least in part. A suicidal urge leads to a homicidal act. This may be followed by two types of reaction which are usually mixed in some combination in each patient: 1. There is an increase in the severity of the symptoms, resulting in either a severe depression, stupor, a Ganser syndrome or catatonic excitement, which in some way may represent a punishment for the deed. 2. There may be a tendency to recover from the symptoms that preceded and led to the deed. Murder of a child is an expression in the parent of a suicidal urge directed against the child which is identified at least in part with the parent.

DISCUSSION

DR. MENAS S. GREGORY: In many cases when a mother with a manic-depressive psychosis attempts to commit suicide, taking her own child with her, as it were, it happens frequently that the child dies but the mother survives. Cases of this type at times will present medicolegal complications, in that the mother who survives the suicidal attempt frequently recovers shortly after the attempt. It should be stated as a matter of clinical experience that some persons suffering from depression of manic-depressive type may show prompt recovery after such unsuccessful attempts at suicide.

Early in my career I had a striking experience. A patient had been depressed for over a year and a half and there was a question of "chronic melancholia." One day he was found hanging from the window. He received timely assistance and survived; within a few days after this experience he recovered fully and was returned home.

Partial or complete recovery from a depression is particularly apt to follow an unsuccessful attempt at suicide in cases of child murder, unless the attempt has inflicted some serious physical injury on the patient.

I will cite a case to illustrate the medicolegal complications. A young mother, with three children, who had been deserted by her husband and was in desperate straits, economic and otherwise, suffered an attack of depression. She attempted to commit suicide by breathing illuminating gas, taking with her her three children. The mother and children were removed to a hospital; the children died but the mother survived. I saw her shortly after the episode and on examination found that she had practically recovered from the depression. The history obtained from her, as well as from those who knew her, indicated clearly that she had suffered a rather severe depression several months prior to the attempt at suicide. It was difficult for me to convince the district attorney or the court that this mother had undoubtedly been psychotic when she attempted to commit suicide by breathing illuminating gas, an attempt which resulted in the death of the children; in fact, it was insisted that she be tried before a jury; this was done and she was acquitted on the ground that at the time she was not of sound mind.

The first important point, therefore, is to remember always that in cases of child murder and attempt at suicide the mother may recover shortly or immediately after such an attempt, and that she may be charged with murder, particularly if there is any semblance of a motive such as some difficulty with her husband or interest in another man. I recall several cases of this kind.

The schizophrenic patient (case 2) has shown and now shows distinct evidence of a Ganser syndrome. Many prisoners, with the motive of escaping or as a means of protection, manifest a Ganser syndrome, especially those with a schizoid make-up. It is very rare, however, that a patient with definite schizophrenia, such as this one presents, resorts to a mechanism of the type of the Ganser syndrome. This observation has diagnostic importance: The Ganser syndrome superimposed on schizophrenia of acute onset may obscure the diagnosis of the more serious underlying disease.

DR. A. A. BRILL: When I listened to Dr. LaMar's presentation, I said to myself, "Dr. LaMar likes to use euphemisms." He said that he practiced psychotherapy, whereas what he did was certainly psychoanalytic, because in no other system of therapy does one find any such approach as he used. His case showed a wish tendency with a very definite basis, which was cured through a psychoanalytic approach.

The case presented by Dr. Katz and discussed by Dr. Harris did not impress me as one that had anything to do with diabetes. Diabetes has been a familiar disease from time immemorial, and if there is a connection between diabetes and psychosis it is strange that no psychiatrist or any one else has ever noted the connection. As expressed by Dr. Cheney, the psychosis was some organically tinged condition, but it had nothing to do with diabetes.

Dr. Bender's cases were of interest; I agree with Dr. Gregory that such murders are based on identification of the parent with the child. I can mention, however, a recent case in which a son attempted suicide and almost stabbed himself to death because he wanted to kill his father. The patient was schizophrenic, aged 30, and fully understood the mechanism of identification. He told me that it was not an honest suicide. For years he had wanted to kill his father; shortly before the suicidal attempt he had the impulse to knock his father down with an oar while he was rowing with him, so that he had to throw the oar into the water to stifle this strong impulse. He stabbed himself because he identified himself with his father.

DR. MEYER M. HARRIS: I wish to comment on the use of old statistics as to the possible relationship of diabetes to a psychosis. As I indicated before, it is unlikely that mild or moderate diabetes plays any rôle. However, with the discovery and use of insulin it has been possible to treat patients with severe diabetes in impending or actual coma. In patients who have been in such a state for some time and have been brought back to life by insulin, the severe metabolic disturbance may lead to some organic trauma on a metabolic basis, recovery from which may take some time. One sees that, for instance, in regard to the carbohydrate tolerance. It may be a week before this comes back to its previous state, when a patient has been permitted to develop severe acidosis.

CHICAGO NEUROLOGICAL SOCIETY

Regular Meeting, Oct. 19, 1933

PERCIVAL BAILEY, M.D., *President, Presiding*

PRESIDENTIAL ADDRESS: THE RELATION OF NEUROLOGY TO OTHER BRANCHES OF MEDICAL PRACTICE. DR. PERCIVAL BAILEY.

A MEMORIAL TO DR. RICHARD S. DEWEY (1845-1933). DR. ARTHUR R. ROGERS, Oconomowoc, Wis.

To have lived eighty-eight years; to have been inspired by high ideals and to have achieved most of them; to have elevated the standards of his chosen profession; to have won and maintained the respect and confidence of his colleagues

as well as of the public; to have possessed a clear mind to the end, and finally, to have met death unflinchingly—these were the achievements of Dr. Richard S. Dewey.

Born on Dec. 6, 1845, at Forestville, N. Y., he was the son of Elijah Dewey, Jr., and the grandson of Elijah Dewey, Sr., a revolutionary soldier. His mother was Sophia Smith, whose father, Richard Smith, was a member of the New York state legislature.

He was married twice, first, in 1873, to Lillian Dwight, a great-granddaughter of Timothy Dwight, who was at one time president of Yale. She died in 1880. He later married Mary E. Brown, who survives him. There were three children by the first marriage, two of whom are living. By the second marriage there were two children, both of whom are living.

Dr. Dewey received his early education in the local district and high schools at Clinton, N. Y. He entered the academic department of the University of Michigan in 1864, remaining until 1866, when he matriculated in the medical department. He received the degree of Doctor of Medicine three years later. He became a Sigma Phi in 1865 and was a loyal and active member throughout his life.

His first medical appointment was that of resident physician at the Brooklyn City Hospital, where he served for twelve months. In 1870, when the Franco-Prussian War broke out, he was appointed volunteer assistant surgeon in the German army. A desire for adventure and a knowledge of the German language made this possible. After several months in the service he was honorably discharged and awarded a medal "Für Pflichttreue im Kriege." He remained abroad for a time, studying microscopy and pathology under Virchow.

Why Dr. Dewey chose psychiatry as a career I have never learned, but in 1871 he was assistant physician at the hospital for the insane at Elgin, Ill. In 1879, he became superintendent of the hospital at Kankakee, Ill. At that time the hospital was in the course of construction, and a notable experiment was being made in operating with separate buildings for different groups of patients. Although Dr. Dewey had no precedent to follow, his management proved an outstanding success. Later, to his undying fame, he introduced for the first time in Illinois the practice of nonrestraint, replacing restraint, which had been much abused in former years.

When in 1893 the turn of the political wheel brought the opposition party into power, Dr. Dewey was obliged to resign.

Beginning in September, 1895, for twenty-five years Dr. Dewey was medical director of the Milwaukee Sanitarium. During these years much of his creative work was done. He was elected president of the American Medico-Psychological Association and was editor of its official publication the *Journal of Insanity*. He was a member of this society (and at one time its president), of the Wisconsin State Medical Society, and a number of local medical organizations, being the president of some.

He was an indefatigable student throughout his life and he maintained his interest in medical subjects until his death, presenting more than forty papers at various medical gatherings.

It is customary to think of an unusually versatile man as being unstable. Dr. Dewey was certainly an exception. However, he could easily have achieved success in the ministry or in any branch of the teaching profession. Success in the field of medicine did not prevent the outcropping of an innate artistic and musical sense. In 1913 he wrote the words and music of a patriotic anthem, "Thou Mighty Nation," which he dedicated to the Mendelssohn Club of Chicago, and which was sung by that organization. During the World War, he composed both the words and the music to a song entitled "Starry Flag." At his funeral, all the music played was of his own composition.

Elsewhere I have spoken of Dr. Dewey's literary ability. He made use of this after his retirement to California by writing his memoirs, which are soon to be published.

My association with Dr. Dewey began in 1895 and extended over a period of ten and one-half years. As assistant physician in the sanatorium at Wauwatosa, Wis., I learned to respect his ability and his remarkable personality; he was gentlemanly and unassuming at all times, and showed an understanding of and a patience with a sick man or woman which was almost uncanny. Much of Dr. Dewey's medical career was sandwiched between the teachings of the old and those of the new schools of psychiatry; yet, as I recall his methods, I believe that in many ways he anticipated the methods and teachings of today. He was always gentle but he showed an ability to be firm as the occasion required and a tendency to give the patient the benefit of the doubt in any question of right or wrong. Dr. Dewey had little sense of time; he was usually late to meals, and barely caught many a train by outside prompting.

I have never known any one else so meticulous in writing. I have seen him write and rewrite a letter several times before being satisfied with its contents. One of his sayings was: "The less you say the less you have to retract." In this and in many other ways he resembled the late Calvin Coolidge.

I am certain that Dr. Dewey was a firm believer in the influence of heredity in the causation of psychoses. After interviewing the relatives of a patient, he was wont to remark, "There is a reason."

In spite of the profundity of Dr. Dewey's mind, he had a great sense of humor —a great asset in treating patients with mental diseases. At many a meeting of his medical fraternity, Alpha Mu Pi Omega, I have seen him convulse his listeners with some humorous poem or a droll article given in a serious strain. His fondness for and his adaptability to people of all ages undoubtedly played a part in his longevity.

My final encomium of Dr. Dewey can be summed up in the following words: Whatever measure of success I may have had in my medical career I attribute to my modest effort to imitate him in principle and in precept.

GREAT NEUROLOGISTS I HAVE KNOWN. DR. HUGH T. PATRICK.

(Dr. Patrick outlined the life and work of Dr. Weir Mitchell, Sir William R. Gowers and Dr. H. Oppenheim.)

SUBDURAL ABSCESS OF THE SPINAL MENINGES. DR. ERIC OLDBERG.

A subdural abscess formed in the lower thoracic portion of the spinal cord. The abscess was associated with osteomyelitis. Operation, with drainage, resulted in recovery of the patient, who formerly had paraplegia.

DISCUSSION

DR. HALE A. HAVEN: A case of mine will perhaps be of interest from the point of view of the possible etiology of the condition. Oppenheim said that such an abscess is always metastatic from a focus of infection elsewhere in the body. Some writers agree with this view, but others disagree, for the chief cause is given as subacute bronchitis.

My patient, a woman, in July, 1932, after trimming her corns had cellulitis of the legs; the inflammation was drained, and she was discharged from the hospital after about four days. About two weeks later she complained of pain in the spine. The family physician found nothing significant except pain along the course of the sciatic nerve. A few weeks later she was thought to have arthritis of the spine. Treatment relieved the pain somewhat, but after a few weeks there was sudden retention of urine, with more pain in the back. She was taken to a hospital, and Dr. Stone found that the knee jerk on one side and the ankle jerks on both sides were absent. Sometime before that a spinal puncture had been done; the fluid was xanthochromic, but the results of tests for the Queckenstedt sign were uncertain. Dr. Stone did a puncture and noted that a few drops of pus escaped from the needle, apparently before the dura had been penetrated. He concluded that there was an extradural abscess in the lumbar region.

The spines of the second and third lumbar vertebrae were removed; the dura appeared normal. With a fine needle inserted through the dura pus was aspirated from within the dural canal. The dura was then incised without opening the arachnoid; at the upper end of the incision an abscess was found among the roots of the cauda, which contained from 5 to 6 cc. of pus. Four months later the patient had entirely recovered, with restoration of all reflexes.

DR. G. B. HASSIN: Where did the capsule of the abscess originate?

DR. ERIC OLDBERG: It was perhaps made up of fibrin.

DR. G. B. HASSIN: The abscess, which possessed a powerful capsule of connective tissue, was probably not subdural but intradural, located in the innermost layers of the dura. Abscesses of the dural spaces usually are epidural and metastatic or arise by extension from disease processes in the vertebrae or other adjacent organs. There are no etiologic facts to justify consideration of metastasis in Dr. Oldberg's case. The dura was evidently damaged by a broken-down vertebra and infected by it, which resulted in a bulging abscess that pressed on the arachnoid. Had the abscess been subdural, that is, above the arachnoid, it would not be possible to explain the origin of the capsule. Where did the capsule originate in Dr. Haven's case?

DR. HALE A. HAVEN: There was no doubt that the abscess in my case was within the arachnoid membrane. It was definitely encapsulated among the roots of the cauda equina. The wall appeared to be a thickened opaque arachnoid, and it certainly had no connection with the dura mater.

Book Reviews

The Visual Fatigue of Motion Pictures. A Worldwide Survey. Edited by Aaron E. Singer. Price, $1. Pp. 48. New York: Amusement Age Publishing Company, 1933.

This booklet is a summary of certain facts connected with the subject and is a survey of the entire field, consisting of a group of short monographs on certain factors of importance in motion pictures. In addition, there is an appendix showing the year-by-year advances in the literature connected with a reduction in the visual fatigue of motion pictures. It is most interesting that the major portion of the literature has appeared since 1930. Not only has the actual amount of writing been greatest in the last three years, but the subjects in these years are far more important.

The part which has to do with the eyes themselves contains an interesting discussion relative to third dimension films. Apparently they are possible for experimental purposes, but they are not considered practical for the theater. In other words, depth in film is not to be anticipated in the moving pictures, at least not on the screens of today. It is problematic whether third dimension films would be easier on the eye. To date, all inventions have pointed in the opposite direction.

The experimenters at the General Electric Company, the Frederick S. Mills & Company and the Westinghouse Lamp Company believe that the effect on eyestrain under the conditions found in most theaters today is relatively inconsequential. Those at the General Neon Tube Corporation state that the blue, green, white and gold lights from neon lamps are the least fatiguing. Prof. A. G. Anderson of the University of Illinois quotes an example relative to fatigue from lighting, and attributes this fatigue to the necessity for the eyes to adjust themselves constantly to the changing intensities of light as presented by the ever-changing film. It is improbable that the inadequate illumination of the average moving picture theater plays a factor in eyestrain. In really modern theaters, where the general illumination is sufficient to permit at least partial recognition of surrounding objects while the moving picture is showing, there should be less fatigue than in houses where it is necessary to have the audience in complete or nearly complete darkness. Any sharp contrast between an object in the direct field of vision and objects in the indirect field of view always leads to fatigue. Orchestra lights, exit lights and other bright points of illumination in an otherwise dark room tend to fatigue, just as a relatively brilliant picture in an otherwise dark room leads to fatigue.

It is not unlikely that moving pictures will bring "to the surface" a refractive error, and unless that is corrected, fatigue and discomfort will result. The flicker which appears under poorer conditions of illumination and projection would undoubtedly be detrimental. Another factor which is to be considered is the rapidly moving scenes in some panoramic and landscape films. Persons with muscular imbalance will occasionally complain of giddiness under these circumstances.

When one considers the many diverse opinions which have appeared in the booklet, it is interesting to note Dr. Frances E. Moscrip's (inspector, Division of Sight and Conservation Classes, New York City) statement relative to the fact that sight conservation classes do not get an official sanction to attend moving pictures. Naturally, there are other factors which control this, but it is relevant. Miss Hazel C. McIntyre of the Ohio State Department of Education states that attendance at movies has been a cause of continued loss of vision in their sight-saving classes.

The subsection on "projection" and the problems connected with this, by Mr. William H. Priess of the International Television Radio Corporation, are abstracted in five subheadings: 1. Fatigue decreases greatly with the increased picture rate.

2. Colored light induces fatigue. 3. Fatigue is induced by a lack of definition. 4. Fatigue is also a factor in the intensity of illumination on the screen. The values now employed in the motion picture field for use in the theater are adequate. The values employed in motion pictures used at home are low. 5. Psychologically, there is relation between fatigue when one has merely a picture alone and fatigue when there is another interest such as sound. Some of these conclusions are not wholly in accord with the opinions of ophthalmologists and optometrists.

The other sections of the booklet consider the relationship which the movies have to education, a brief discussion of ventilation in moving picture theaters, the architecture of moving picture theaters, seating and posture, physical features connected with the screen itself and a very brief discussion of special spectacles for the movies. There is no doubt that the seating in many theaters is wretched. The seats are, however, no worse than those in the legitimate theaters. A statement of Dr. Ralph H. Williams is of interest in connection with this. "Some are so bad that the patron leaves the theater in a state of muscular tension throughout the entire body as a result of two and one-half to three hours of enforced discomfort, which does no good to the general nervous system. The normal individual with a stable nervous system will throw off this tension entirely with a normal night's rest, but the individual with an unstable nervous system will not so readily return to normal and with too frequent repetitions of such strains will develop increased irritability."

Mass und Zahl in der Pathologie. By R. Roessle and F. Roulet. Price, 17.40 marks. Pp. 144, with 27 figures. Berlin: Julius Springer, 1932.

The study of human constitution should be based on that of human anatomy, and much more study should be centered on the constitutional variations of the internal organs in healthy and in diseased persons. For twenty years Roessle has been carrying on quantitative autopsies in the hope of determining what lies behind the constitution of a person. His great opportunity came during the World War when numerous healthy young men met with violent death and showed good preservation of the internal organs. First, at Jena, and more recently at Berlin, he has been carrying on this work, and the results, as well as those of other work reported in the literature, are published in this small volume of the Aschoff series of monographs.

Starting with corporeal development as a whole, the authors single out the various organs, studying their variations particularly with regard to changes resulting from growth and involution. Included are the endocrine glands, the nervous system and the voluntary musculature. Too little work has thus far been done on organ correlations to render them very useful. At the end of the book is their series of sample cases (*Musterfälle*) which showed harmonious development without terminal wasting. The authors desire to extend their observations and to combine them with measurements taken during life of the school children and of the recruits, in order to construct still more exact pictures. Taking up where the physical anthropologist leaves off, the interior of the body must be investigated. Moreover, when types have been established and the diseases peculiar to each have been set forth, constitution will once more take the place it formerly held in the realms of prognosis and therapeutics.

While the changes caused by age in some organs are striking during the period of senescence and decay, the number of aged persons seems too small to permit of valid conclusions. Moreover, the general wasting of the whole body after 70 is not accorded sufficient prominence, and the tail ends of the curves are misleading when the large figures for probable error are read from the accompanying tables. More space should have been given to variations in the weight of organs with the weight of the body, and some studies of correlations of the weights of organs and stature would have been interesting. Finer division of the material into body types, into disease types and into psychologic types was not attempted, yet it would seem that if a constitutional pathology were to be inaugurated these subdivisions

would be of great significance. On the other hand, the authors have taken care to separate the material according to age and sex, and they have excluded organs that were considered diseased. The statistical handling of the material is satisfactory. Aside from its value to the student of constitution, the book will be useful to the pathologist, since it shows not only what the average size of a certain organ is, but also the normal variations to be expected at a given age. A useful bibliography and numerous charts and tables accompany the text.

Set the Children Free. By Fritz Wittels. Translated by Eden and Cedar Paul. Price, $2.75. Pp. 242. New York, W. W. Norton & Company, Inc., 1933. (The translation has been made from the fourth German edition (1927) of Die Befreiung des Kindes, specially revised and brought up to date by the author in 1932.)

The author is a prominent psychoanalyst, and this is not his first successful work in psychoanalytic and psychiatric literature. This work pertains entirely to children and child life, and is written almost entirely from a psychoanalytic point of view. Frequent reference is made, however, to Jean Jacques Rousseau and it is felt throughout that the principles of the education of children as advanced by Rousseau give the author as much material as does his freudian background. The development of the mental and emotional life, the ego, the personality and every possible detail concerning the child is gone into exhaustively. Active correlation of psychoanalytic theories and practices with the daily problems and technic of handling children is frequently attempted. It is doubtful whether there is in print a clearer, simpler presentation of the psychoanalytic principles and point of view than is contained in this book. It is exceptionally clearcut, particularly in explaining to lay readers facts regarding the development of the child. The most antagonistic of nonpsychoanalytic groups cannot help but understand the simplicity and logic of statements, particularly those found in chapter 7. It is true that the statements are often dogmatic and imply no exception, but this is probably because of the simplicity of presentation. Chapter 4, on Doubt, is a practical discussion of the relationship of parent to child. In chapter 5, the old idea of the child losing interest or forgetting unpleasant experiences is explained as being not a passive process, but an active process of repression.

Chapter 9 is a most striking story of one family. It is an extreme example, but it effectively shows the forces present in many family groups. It is clear that the author believes in the removal of a child from any bad environmental situation if the problems are very critical. He is an advocate of the "children's houses" (Montessori). Chapter 8, somewhat bitter throughout, is a discussion of the keynote of the book. The child is considered to be a slave in many respects, and the advice is given that one should love children and keep oneself so related to them that one leaves them, although outwardly disciplined, inwardly free, and worthy of their love and honor, without forcing it. One suspects that personal experience in early life, as well as clinical experience of this author in later life, is involved in the strength and directness of this book.

It is a good book for parents and teachers to read, as well as for other workers who have contact with the training or handling of children.

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